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(54) Benzamide derivatives and their use as vasopressin antagonists

Benzamid-Derivate und ihre Verwendung als Vasopressin-Antagonisten

Dérives de benzamide et leur utilisation comme antagonistes de vasopressine

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(56) References cited:
EP-A- 0 514 667 **WO-A-91/05549**

Remarks:
The file contains technical information submitted after the application was filed and not included in this specification

EP 0 620 216 B1

Description

[0001] This invention relates to new benzamide derivatives and pharmaceutically acceptable salts thereof.

[0002] More particularly, it relates to new benzamide derivatives and pharmaceutically acceptable salts thereof which possess activities as vasopressin antagonistic activity, vasodilating activity, hypotensive activity, activity for inhibiting saccharide release in liver, activity for inhibiting growth of mesagium cells, water diuretic activity, platelet agglutination inhibitory activity, oxytocin antagonistic activity and the like, to a pharmaceutical composition comprising the same for the treatment and/or prevention of hypertension, heart failure, renal insufficiency, edema, ascites, vasopressin parasecretion syndrome, hepatocirrhosis, hyponatremia, hypokalemia, diabetic, circulation disorder, oxytocin relating diseases [e.g. premature delivery, dysmenorrhea, endometritis, etc.] and the like in human beings or animals.

[0003] One object of this invention is to provide new and useful benzamide derivatives which possess aforesaid activities.

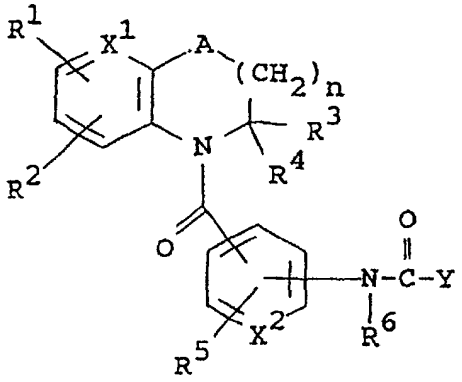
[0004] Another object of this invention is to provide processes for the preparation of said benzamide derivatives and salts thereof.

[0005] A further object of this invention is to provide a pharmaceutical composition comprising, as an active ingredient, said benzamide derivatives and pharmaceutically acceptable salts thereof.

[0006] Still further object of this invention is to provide a use of the compounds of the invention for the manufacture of a medicament for the treatment and/or prevention of aforesaid diseases in human beings or animals, using said benzamide derivatives and pharmaceutically acceptable salts thereof.

[0007] Some benzamide derivatives have been known as vasopressin antagonist or oxytocin antagonist, for example, in International Publication Nos. WO 91/05549 and WO 94/01113, and Japanese Patent Application Publication Nos. 5-132466 and 5-320135.

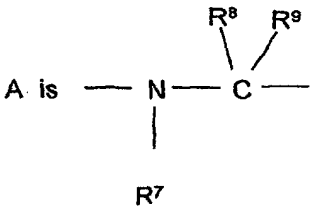
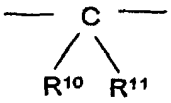
[0008] The object benzamide derivatives of this invention are new and can be represented by the following general formula (I) :



(I)

wherein

R^1	is hydrogen or (C_1-C_6) alkyl,
R^2	is hydrogen, (C_1-C_6) alkyl, halo (C_1-C_6) alkyl, halogen or (C_1-C_6) alkoxy,
R^3 and R^4	are each hydrogen, (C_1-C_6) alkyl or taken together to form oxo,
R^5	is hydrogen, halogen, nitro, hydroxy, (C_1-C_6)alkoxy(C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkoxy(C_1-C_6)alkoxy, phenyl(C_1-C_6)alkoxy, nitrophenyl(C_1-C_6)alkoxy, (C_1-C_6)alkanoyloxy, benzoyloxy, fluorenecarbonyloxy, (C_1-C_6)alkoxycarbonyloxy, phenyl(C_1-C_6)alkoxycarbonyloxy, halophenyl(C_1-C_6)alkoxycarbonyloxy, tri(C_1-C_6)alkylsilyloxy, (C_1-C_6) alkyl or (C_1-C_6) alkoxy optionally substituted with (C_1-C_6)alkylamino,
R^6	is hydrogen, (C_1-C_6) alkyl or (C_1-C_6) alkoxycarbonyl,
A	is

A is  or 

in which

R^7 is hydrogen; (C_1-C_6) alkyl optionally substituted with halogen, amino, (C_1-C_6) alkylamino, (C_1-C_6)alkanoylamino, halo(C_1-C_6)alkanoylamino, phthaloylamino, (C_1-C_6)alkoxycarbonylamino, benzyloxycarbonylamino, nitrobenzyloxycarbonylamino, benzenesulfonylamino, tosylamino, nitrophenylsulfenylamino, tritylamino, benzylamino, carboxy, (C_1-C_6)alkoxycarbonyl, di(C_1-C_6)alkylamino(C_1-C_6)alkoxycarbonyl, halo(C_1-C_6)alkoxycarbonyl, trihalo(C_1-C_6)alkoxycarbonyl, phenoxycarbonyl, nitrophenoxycarbonyl, naphthyloxycarbonyl, phenyl(C_1-C_6)alkoxycarbonyl, nitrophenyl(C_1-C_6)alkoxycarbonyl, carbamoyl, (C_1-C_6) alkylcarbamoyl, trihalo(C_1-C_6)alkanoyl, unsubstituted (C_1-C_6) alkanoyl, toluoyl, di(tert-butyl)benzoyl, tolylbenzoyl, aminobenzoyl, tolylbenzoylaminobenzoyl, unsubstituted benzoyl, an N-containing heterocyclic carbonyl, (C_1-C_6) alkylsulfonyl, tolylsulfonyl, di(C_1-C_6)alkoxyphenylsulfonyl, unsubstituted phenylsulfonyl, piperidyl, pyridyl, N-(C_1-C_6) alkylpiperazinyl, hydroxy, (C_1-C_6)alkoxy(C_1-C_6)alkoxy, (C_1-C_6) alkoxy(C_1-C_6)alkoxy(C_1-C_6)alkoxy, phenyl(C_1-C_6)alkoxy, nitrophenyl(C_1-C_6)alkoxy, (C_1-C_6)alkanoyloxy, benzoyloxy, fluorenecarbonyloxy, (C_1-C_6)alkoxycarbonyloxy, phenyl(C_1-C_6)alkoxycarbonyloxy, halophenyl(C_1-C_6)alkoxycarbonyloxy, tri(C_1-C_6)alkylsilyloxy or dimethoxyphenylsulfonyl; and

R^8 and R^9 are taken together to form oxo or thioxo;

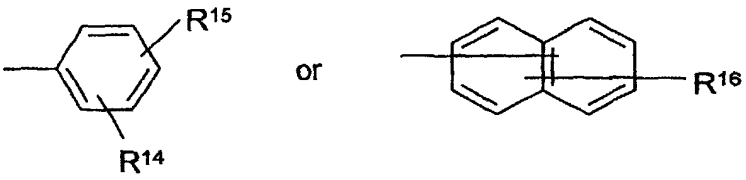
R^{10} is hydrogen;

R^{11} is hydrogen, or (C_1-C_6)alkylamino;

X_1 is CH,

X_2 is CH or N,

Y is



in which

R^{14} is hydrogen, halogen, hydroxy or (C_1-C_6) alkoxy,

R^{15} is phenoxy, naphthyl, phenyl substituted with substituent(s) selected from the group consisting of (C_1-C_6) alkyl, (C_1-C_6) alkoxy, halogen, halo (C_1-C_6) alkyl, hydroxy, amino (C_1-C_6) alkyl, azido (C_1-C_6) alkyl, (C_1-C_6) alkylamino (C_1-C_6) alkyl, (C_1-C_6) alkanoylamino (C_1-C_6) alkyl, hydroxy (C_1-C_6) alkyl, cyano, carboxy, (C_1-C_6)alkoxycarbonyl, di(C_1-C_6)alkylamino(C_1-C_6)alkoxycarbonyl, halo(C_1-C_6)alkoxycarbonyl, trihalo(C_1-C_6)alkoxycarbonyl, phenoxycarbonyl, nitrophenoxycarbonyl, naphthyloxycarbonyl, phenyl(C_1-C_6)alkoxycarbonyl, nitrophenyl (C_1-C_6)alkoxycarbonyl, pyridyl or pyrrolyl, and

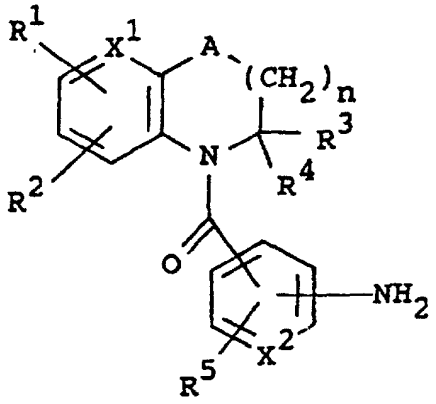
R^{16} is tolyl and

n is 0, 1, 2 or 3,

and pharmaceutically acceptable salts thereof.

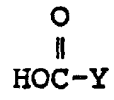
[0009] The object compound (I) or its salt can be prepared by the processes as illustrated in the following reaction schemes.

Process 1

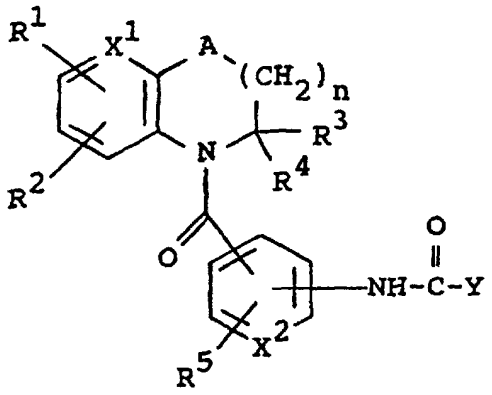


(II)
or its salt

+

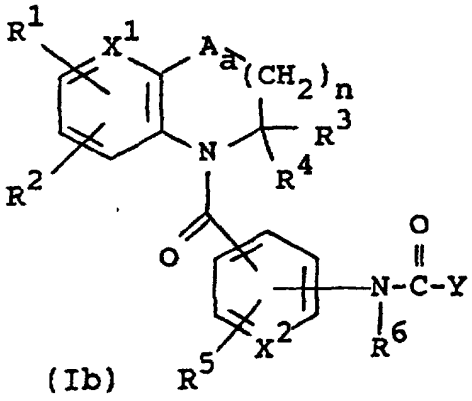


(III)
or its reactive derivative
at the carboxy group
or a salt thereof



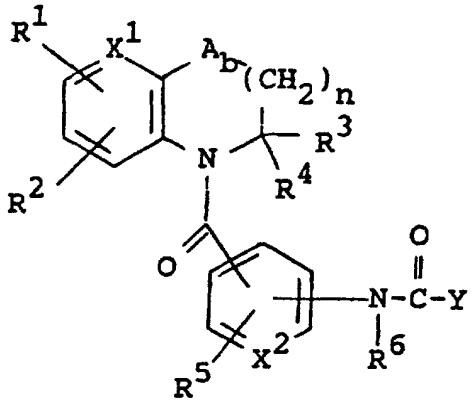
(Ia)
or its salt

Process 2



(Ib)

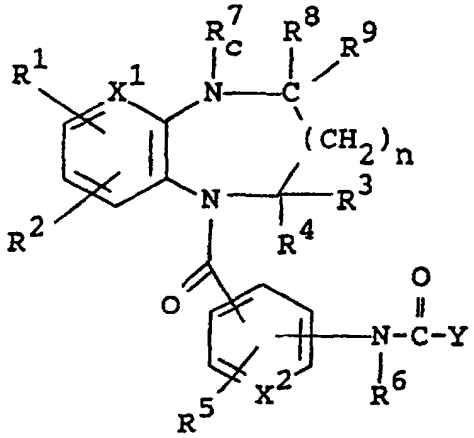
or its reactive derivative
at the carboxy group
or a salt thereof



(Ic)

or its salt

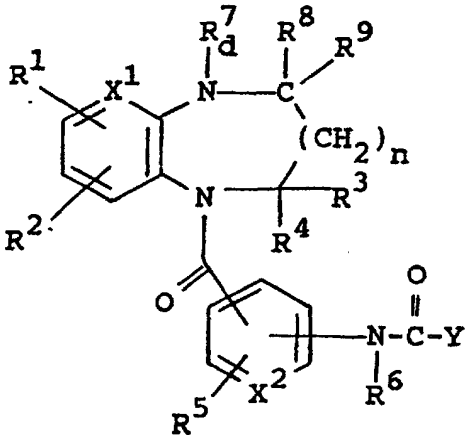
Process 3



elimination of the N-protective group

(Id)

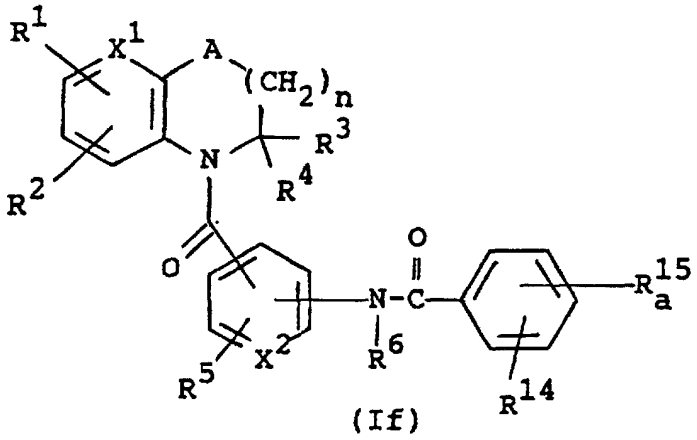
or its salt



(Ie)

or its salt

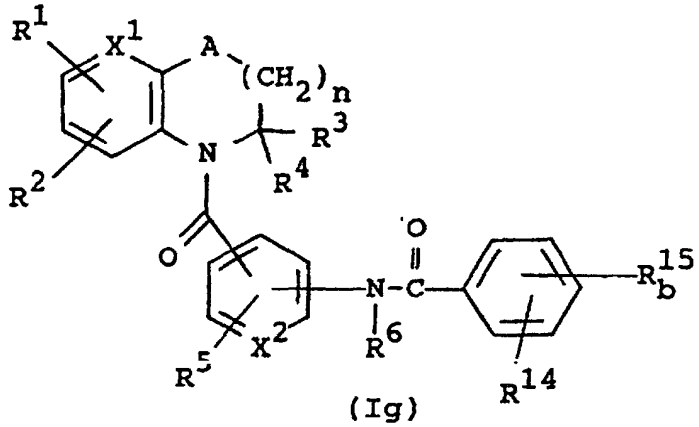
Process 4



reduction

(If)

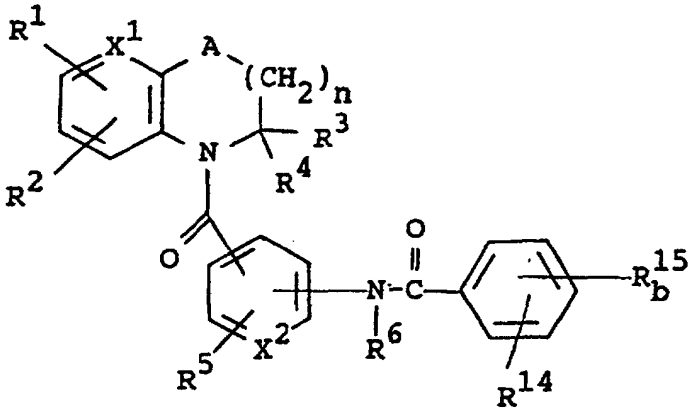
or its salt



(Ig)

or its salt

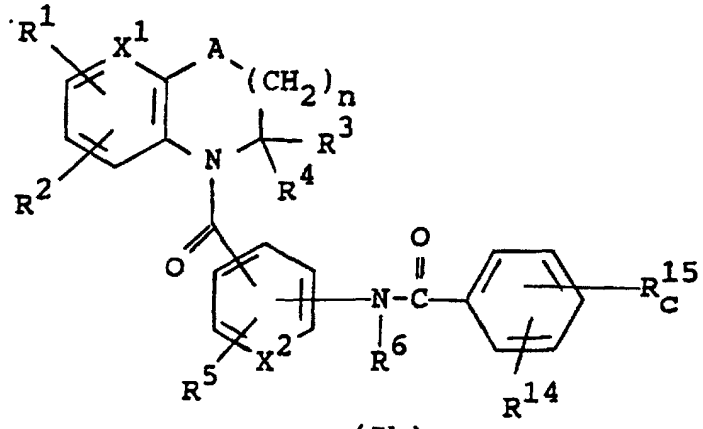
Process 5



acylation

(Ig)

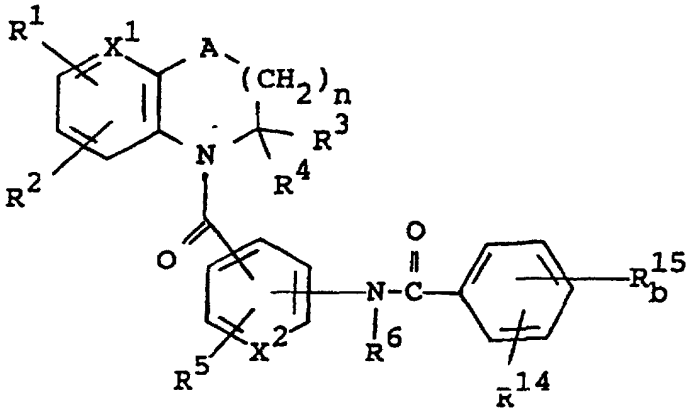
or its salt



(Ih)

or its salt

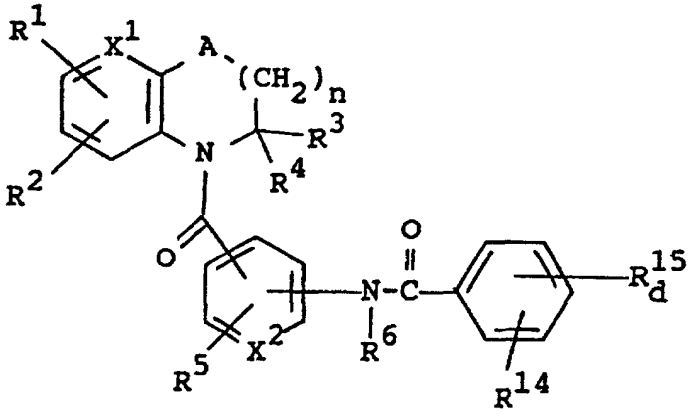
Process 6



alkylation

(Ig)

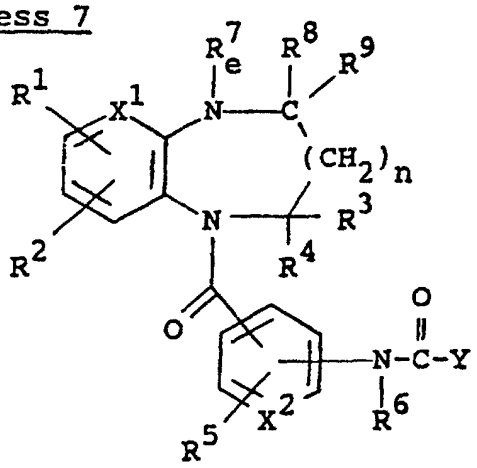
or its salt



(Ii)

or its salt

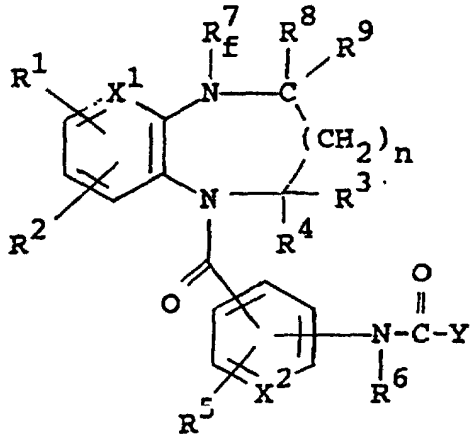
Process 7



alkylation

(Ij)

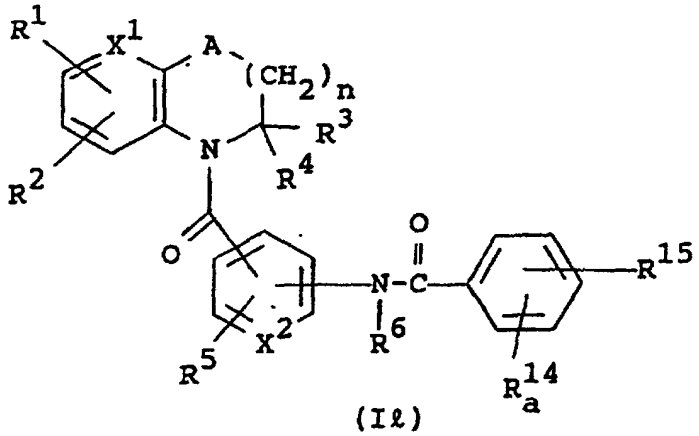
or its salt



(Ik)

or its salt

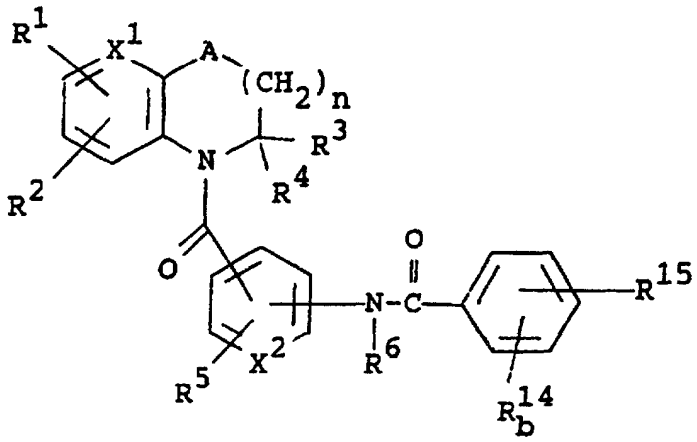
Process 8



dealkylation

(Iℓ)

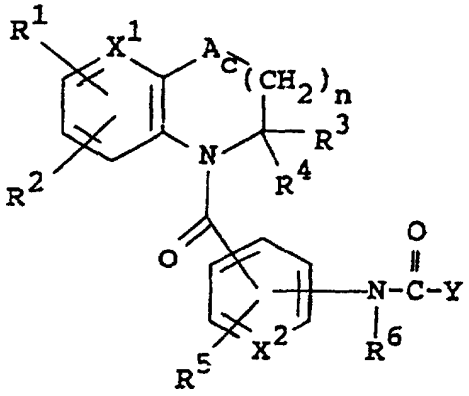
or its salt



(Im)

or its salt

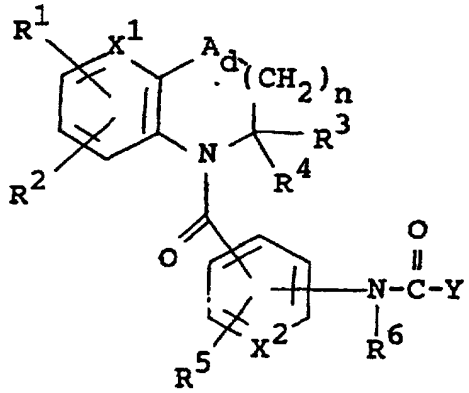
Process 9



deesterification

(In)

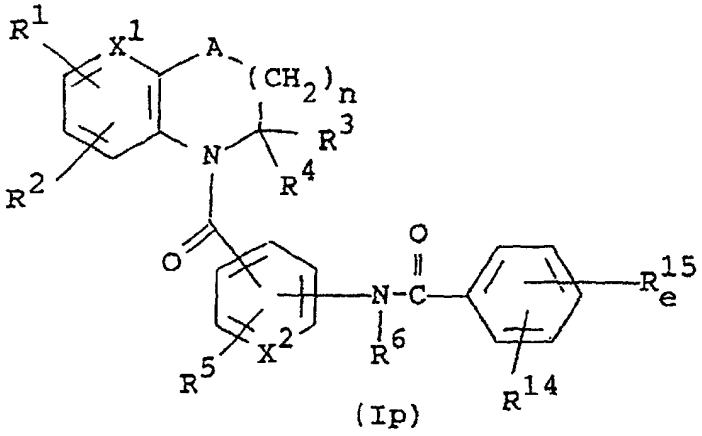
or its salt



(Io)

or its salt

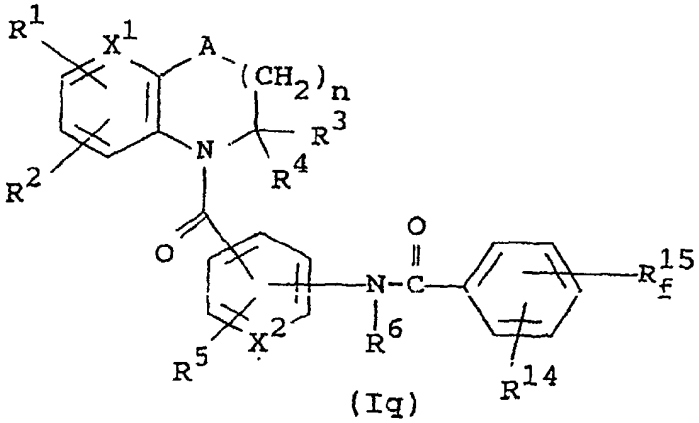
Process 10



esterification

(Ip)

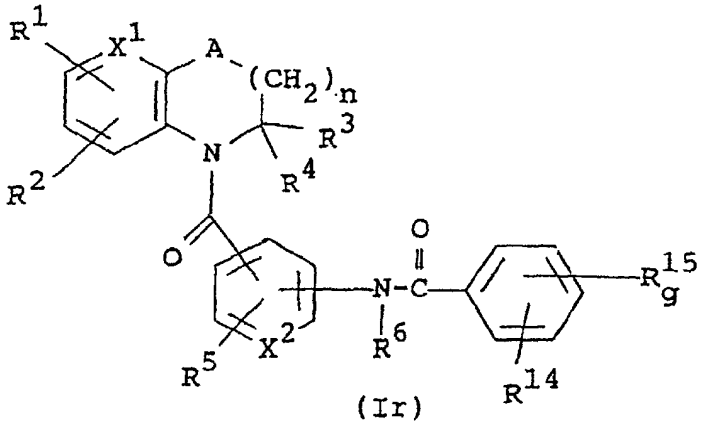
or its reactive derivative at the carboxy group or a salt thereof



(Iq)

or its salt

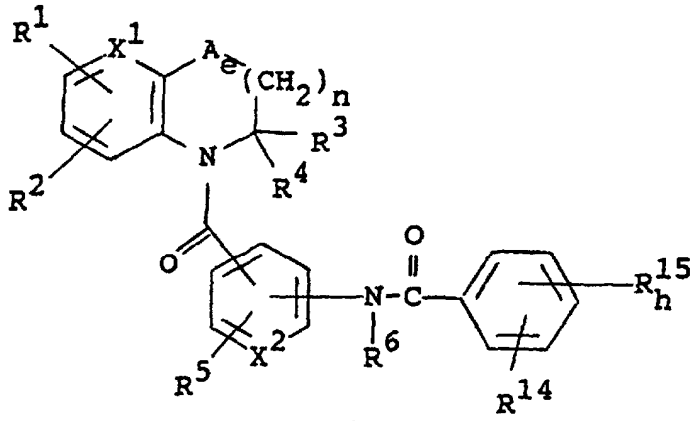
Process 11



reduction

(Ir)

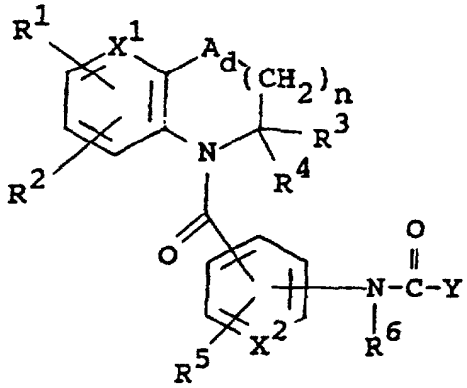
or its salt



(Is)

or its salt

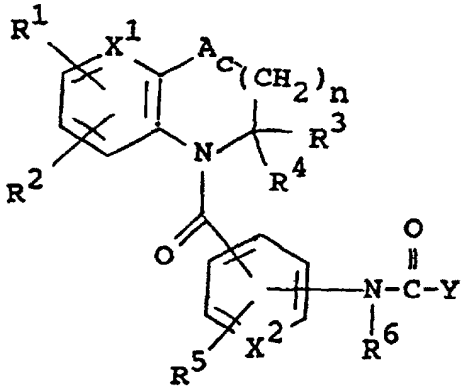
Process 12



esterification

(Io)

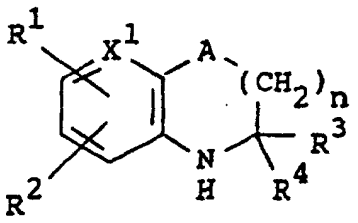
or its reactive derivative at the carboxy group or a salt thereof



(In)

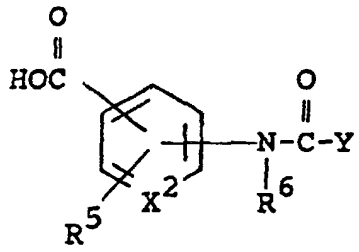
or its salt

Process 13

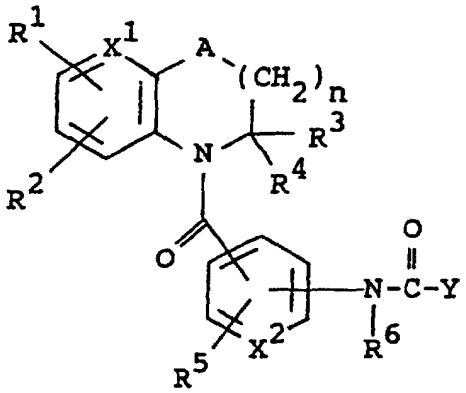


(IV)
or its salt

+

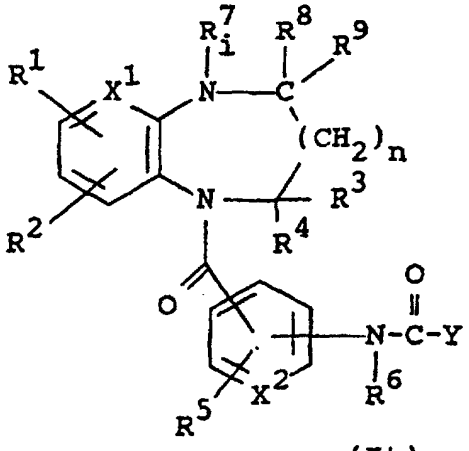


(V)
or its reactive derivative at the carboxy group or a salt thereof



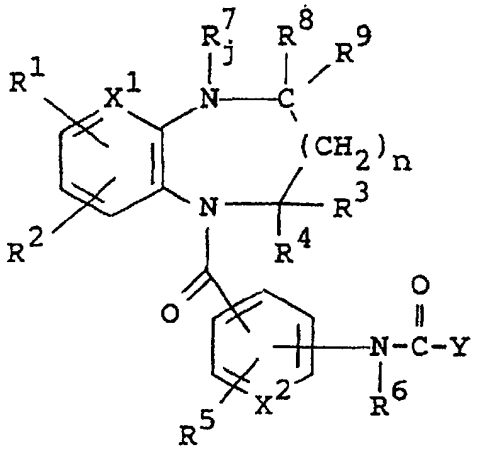
(I)
or its salt

Process 14



(It)
or its salt

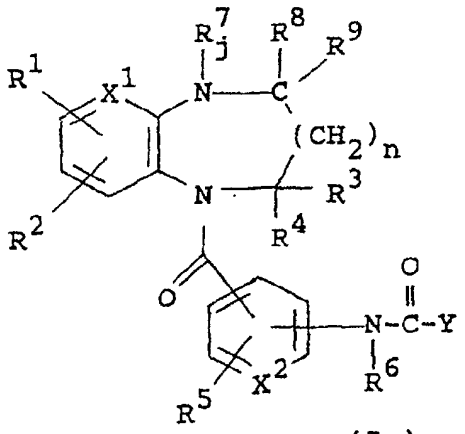
elimination of hydroxy protective group



(Iu)

or its salt

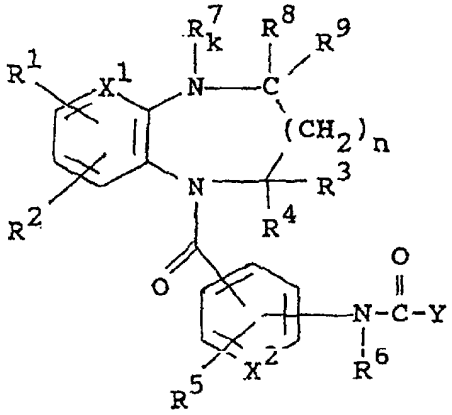
Process 15



oxidation

(Iu)

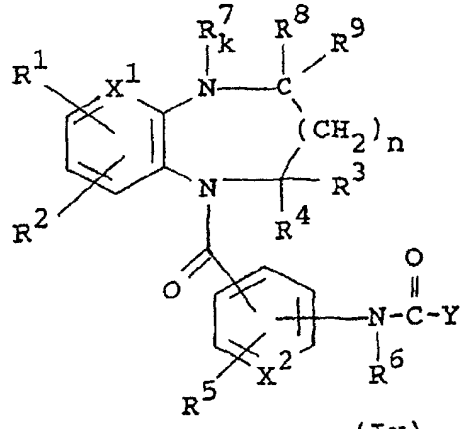
or its salt



(Ix)

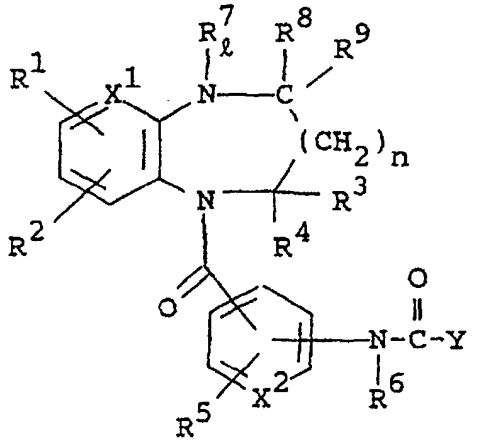
or its salt

Process 16



(Ix)

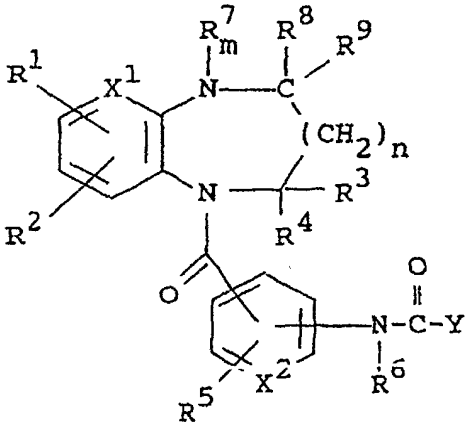
or its salt



(Iy)

or its salt

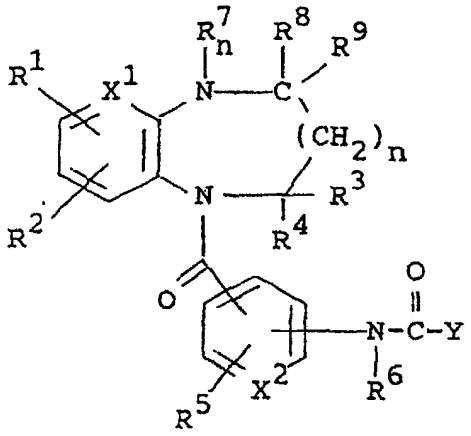
Process 17



acylation

(Iz)

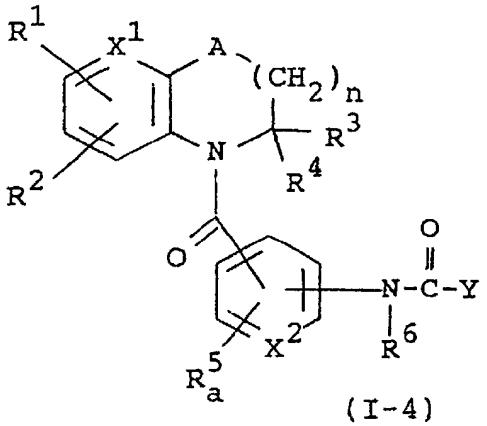
or its salt



(I-1)

or its salt

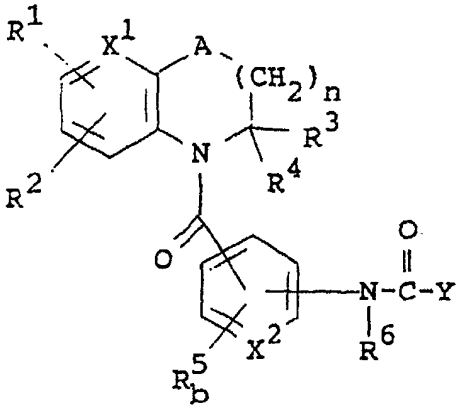
Process 18



alkylation

(I-4)

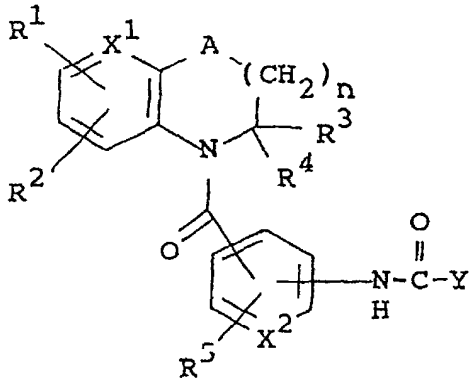
or its salt



(I-5)

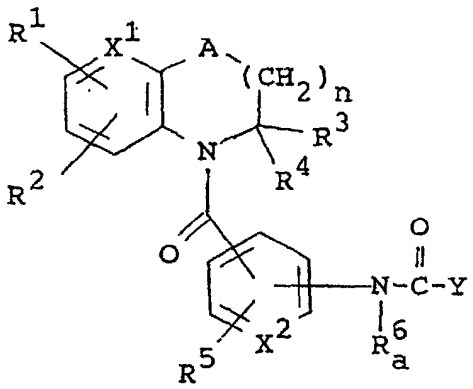
or its salt

Process 19



(Ia)

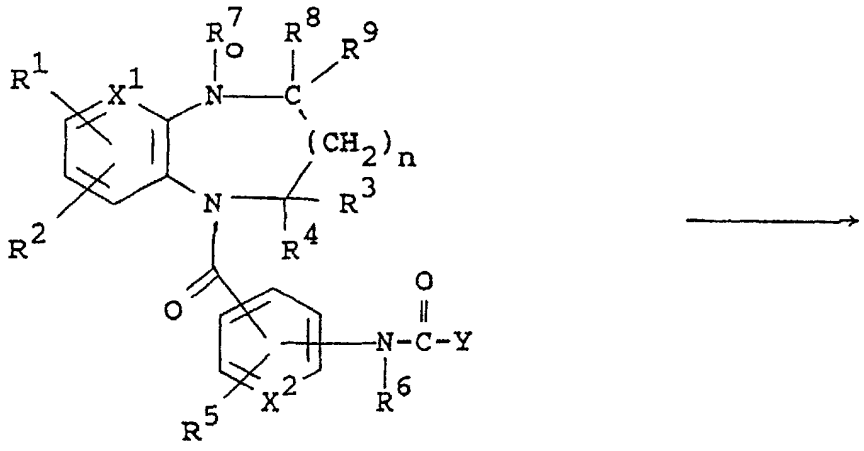
or its salt



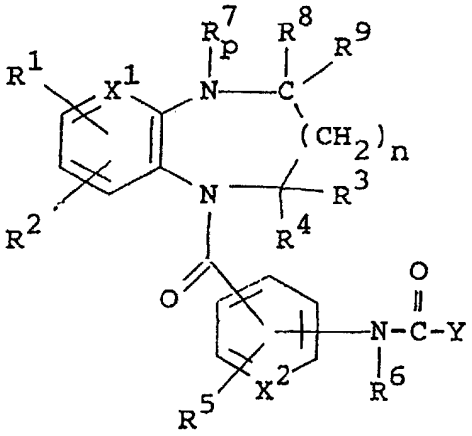
(I-6)

or its salt

Process 20



(I-7)
or its salt

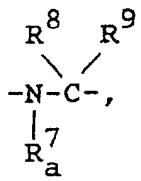


(I-8)
or its salt

wherein

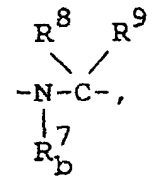
R^1, R^2, R^3, R^4, R^5, R^6, A, X^1, X^2, Y and n are each as defined above,

A_a is



in which

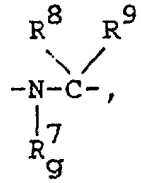
R^8 and R^9 are each as defined above;
R^7 is lower alkyl substituted with carboxy;
A_b^a is



in which

R^8 and R^9 are each as defined above;
R^7_b is lower alkyl substituted with carbamoyl which may be substituted with lower alkyl or an N- containing heterocycliccarbonyl;
R^7 is lower alkyl substituted with protected amino or N-protected piperazinylcarbonyl,
$R^{7'}$ is lower alkyl substituted with amino or piperazinylcarbonyl,
$R^{\phi 5}$ is phenyl substituted with azido(lower)alkyl,
$R^{\phi 5}$ is phenyl substituted with amino(lower)alkyl,
$R^{\phi 5}$ is phenyl substituted with acylamino(lower)-alkyl,
$R^{\phi 5}$ is phenyl substituted with lower alkylamino-(lower)alkyl,
$R^{4'}$ is lower alkyl substituted with amino,
$R^{4'}$ is lower alkyl substituted with lower alkylamino,
$R^{\phi 4}$ is lower alkoxy,
$R^{\phi 4}_b$ is hydroxy,

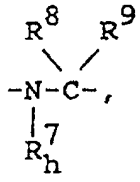
A_c is



in which

R^8 and R^9 are each as defined above;
R^7_g is lower alkyl substituted with esterified carboxy or N-[esterified carboxy(lower)alkyl]piperazinylcarbonyl;

A_d is



in which

R^8 and R^9 are each as defined above,

R^{7} is lower alkyl substituted with carboxy or N-[carboxy(lower)alkyl]piperazinylcarbonyl,
R^{15} is phenyl substituted with carboxy,
R^{25} is phenyl substituted with esterified carboxy,
R^{15} is phenyl substituted with carboxy or esterified carboxy,
R^{25} is phenyl substituted with hydroxymethyl,
R^{7} is lower alkyl substituted with protected hydroxy,
R^{7} is lower alkyl substituted with hydroxy,
R^{7} is lower alkyl substituted with formyl,
R^{8} is lower alkyl substituted with di(lower)-alkylamino or N-containing heterocyclic group,
R^{7} is lower alkyl substituted with N-[hydroxy-(lower)alkyl]piperazinylcarbonyl,
R^{7} is lower alkyl substituted with N-[acyloxy-(lower)alkyl]piperazinylcarbonyl,
R^{9} is lower alkylthio optionally substituted with lower alkylamino,
R^{8} is hydroxy,
R^{8} is lower alkoxy optionally substituted with lower alkylamino,
R^{9} is lower alkyl or acyl,
R^{4} is lower alkyl substituted with N-lower alkylpiperazinylcarbonyl, and
R^{9}_{p} is lower alkyl substituted with N,N-di(lower alkyl)piperaziniocarbonyl.

[0010] In the above and subsequent description of the present specification, suitable examples of the various definitions to be included within the scope of the invention are explained in detail in the following.

[0011] The term "lower" is intended to mean a group having 1 to 6 carbon atom(s), preferably one having 1 to 4 carbon atom(s), unless otherwise provided.

[0012] Suitable "lower alkyl" and lower alkyl moiety in the terms "halo(lower)alkyl", "amino(lower)alkyl", "N-lower alkylpiperazinyl", "lower alkylthio", "N-[esterified carboxy(lower)alkyl]piperazinylcarbonyl", "N-[carboxy(lower)alkyl]piperazinylcarbonyl", "N-[hydroxy(lower)alkyl]piperazinylcarbonyl", "N-[acyloxy(lower)alkyl]piperazinylcarbonyl", "N-lower alkylpiperazinylcarbonyl", "N,N-di(lower alkyl)-piperaziniocarbonyl", "a heterocyclic(lower)alkyl", "N-[amino(lower)alkyl]piperazinylcarbonyl", "N-[protected amino(lower)alkyl]piperazinylcarbonyl", "lower alkylsulfonyl", "azido(lower)alkyl", "lower alkylamino(lower)alkyl", "acylamino(lower)alkyl", "hydroxy(lower)alkyl", "lower alkylcarbamoyl", "acyl(lower)alkyl" and "lower alkylamino" may be straight or branched one such as methyl, ethyl, propyl, isopropyl, butyl, isobutyl, tert-butyl, pentyl, hexyl, in which preferable one is C_1-C_4 alkyl such as methyl, ethyl, propyl, isobutvl or tert-butyl.

[0013] Suitable "aryl" and aryl moiety in the terms "aryloxy" and "arylsulfonyl" may be phenyl, naphthyl, phenyl substituted with lower alkyl [e.g. tolyl, xylyl, mesityl, cumenyl, di(tert-butyl)phenyl, etc.], in which preferable one is phenyl or tolyl.

[0014] Suitable "halogen" may be fluorine, chlorine, bromine and iodine, in which preferable one is fluorine or chlorine.

[0015] Suitable "lower alkoxy" and lower alkoxy moiety in the term "lower alkoxyimino" may be methoxy, ethoxy, propoxy, isopropoxy, butoxy, in which preferable one is methoxy or propoxy.

[0016] Suitable "lower alkylamino" may be mono or di(lower alkyl)amino such as methylamino, ethylamino, propylamino, isopropylamino, butylamino, tert-butylamino, isobutylamino, pentylamino, hexylamino, dimethylamino, diethylamino, dipropylamino, dibutylamino, diisopropylamino, dipentylamino, dihexylamino, N-methylethylamino, in which preferable one is dimethylamino.

[0017] Suitable "lower alkylamino(lower)alkyl" may be mono or di(lower alkyl)amino substituted lower alkyl such as methylaminomethyl, methylaminoethyl, methylaminopropyl, methylaminobutyl, methylaminohexyl, ethylaminomethyl, ethylaminoethyl, ethylaminopropyl, ethylaminobutyl, ethylaminohexyl, dimethylaminomethyl, dimethylaminoethyl, dimethylaminopropyl, dimethylaminobutyl, dimethylaminohexyl, diethylaminomethyl, diethylaminoethyl, diethylaminopropyl, diethylaminobutyl, diethylaminohexyl or the like, in which preferable one is dimethylaminoethyl, dimethylaminopropyl or dimethylaminobutyl.

[0018] Suitable "halo(lower)alkyl" may be chloromethyl, fluoromethyl, bromomethyl, difluoromethyl, dichloromethyl, trifluoromethyl, trichloromethyl, 2-fluoroethyl and the like, in which preferable one is trifluoromethyl.

[0019] Suitable "heterocyclic group" and a heterocyclic moiety in the terms "a heterocyclic(lower)alkyl" and "a heterocycliccarbonyl" may be one containing at least one hetero atom selected from nitrogen, sulfur and oxygen atom, and may include saturated or unsaturated, monocyclic or polycyclic heterocyclic group, and preferable heterocyclic group may be N-containing heterocyclic group such as unsaturated 3 to 6 membered heteromonocyclic group containing 1 to 4 nitrogen atoms, for example, pyrrolyl, pyrrolinyl, imidazolyl, pyrazolyl, pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, triazolyl [e.g. 4H-1,2,4-triazolyl, 1H-1,2,3-triazolyl, 2H-1,2,3-triazolyl, etc.], tetrazolyl [e.g. 1H-tetrazolyl, 2H-tetrazolyl, etc.], etc.;
saturated 3 to 7-membered heteromonocyclic group containing 1 to 4 nitrogen atoms [e.g. pyrrolidinyl, imidazolidinyl, piperidyl, piperazinyl, homopiperazinyl, etc.];
saturated heteropolycyclic group containing 1 to 4 nitrogen atoms, for example, quinuclidinyl, etc.; unsaturated con-

densed heterocyclic group containing 1 to 5 nitrogen atoms, for example, indolyl, isoindolyl, indolizinyl, benzimidazolyl, quinolyl, isoquinolyl, indazolyl, benzotriazolyl, tetrazolopyridazinyl [e.g. tetrazolo[1,5-b]pyridazinyl, etc.], etc.;
unsaturated 3 to 6-membered heteromonocyclic group containing an oxygen atom, for example, pyranyl, furyl, etc.;
unsaturated, 3 to 6-membered heteromonocyclic group containing 1 to 2 sulfur atoms, for example, thienyl, etc.;
unsaturated 3 to 6-membered heteromonocyclic group containing 1 to 2 oxygen atoms and 1 to 3 nitrogen atoms, for example, oxazolyl, isoxazolyl, oxadiazolyl [e.g. 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl, 1,2,5-oxadiazolyl, etc.], etc.;
saturated 3 to 6-membered heteromonocyclic group containing 1 to 2 oxygen atoms and 1 to 3 nitrogen atoms [e.g. morpholinyl, etc.];
unsaturated condensed heterocyclic group containing 1 to 2 oxygen atoms and 1 to 3 nitrogen atoms [e.g. benzofurazanyl, benzoxazolyl, benzoxadiazolyl, etc.]; unsaturated 3 to 6-membered heteromonocyclic group containing 1 to 2 sulfur atoms and 1 to 3 nitrogen atoms, for example, thiazolyl, thiadiazolyl [e.g., 1,2,4-thiadiazolyl, 1,3,4-thiadiazolyl, 1,2,5-thiadiazolyl, etc.], etc.;
saturated 3 to 6-membered heteromonocyclic group containing 1 to 2 sulfur atoms and 1 to 3 nitrogen atoms [e.g., thiazolidinyl, etc.];
unsaturated condensed heterocyclic group containing 1 to 2 sulfur atoms and 1 to 3 nitrogen atoms [e.g., benzothiazolyl, benzothiadiazolyl, etc.];
unsaturated condensed heterocyclic group containing 1 to 2 oxygen atoms [e.g. benzofuranyl, benzodioxolyl, etc.] and the like.

[0020] Said "heterocyclic group" may be substituted with lower alkyl optionally substituted with hydroxy, acyloxy, amino, protected amino, acyl, aryl or methylenedioxyphenyl; acyl or a heterocyclic group, in which preferable one is piperazinyl, N-methylpiperazinyl, N,N-dimethylpiperazinio, N-methylhomopiperazinyl, N-(2-hydroxyethyl)piperazinyl, N-(2-acetoxyethyl)piperazinyl, N-(3-phthalimidopropyl)-piperazinyl, N-(3-aminopropyl)piperazinyl, N-(pyrrolidinylcarbonylmethyl)piperazinyl, N-(methylenedioxyphenylmethyl)piperazinyl, N-ethoxycarbonylpiperazinyl, N-carboxypiperazinyl, N-tert-butoxycarbonylpiperazinyl, N-pyridylpiperazinyl, dimethylaminopiperidyl, pyrrolyl, pyridyl, piperidyl, morpholinyl or quinuclidinyl.

[0021] Suitable "acyl" and acyl moiety in the terms "acylamino(lower)alkyl", "acyl(lower)alkyl" and "N-[acyloxy(lower)alkyl]piperazinylcarbonyl" may be carboxy, esterified carboxy, carbamoyl, lower alkylcarbamoyl, lower alkanoyl, aroyl, a heterocycliccarbonyl, lower alkylsulfonyl, arylsulfonyl.

[0022] The esterified carboxy may be substituted or unsubstituted lower alkoxycarbonyl [e.g. methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl, butoxycarbonyl, tert-butoxycarbonyl, hexyloxycarbonyl, 2-(dimethylamino)-ethoxycarbonyl, 2-iodoethoxycarbonyl, 2,2,2-trichloroethoxycarbonyl, etc.], substituted or unsubstituted aryloxycarbonyl [e.g. phenoxycarbonyl, 4-nitrophenoxycarbonyl, 2-naphthyloxycarbonyl, etc.], substituted or unsubstituted ar(lower)alkoxycarbonyl [e.g. benzyloxycarbonyl, phenethyloxycarbonyl, benzhydryloxycarbonyl, 4-nitrobenzyloxycarbonyl, etc.] and the like, in which preferable one is lower alkoxycarbonyl or 2-(dimethylamino)ethoxycarbonyl.

[0023] The lower alkylcarbamoyl may be mono or di(lower)alkylcarbamoyl such as methylcarbamoyl, ethylcarbamoyl, propylcarbamoyl, dimethylcarbamoyl, diethylcarbamoyl, N-methyl-N-ethylcarbamoyl .

[0024] The lower alkanoyl may be substituted or unsubstituted one such as formyl, acetyl, propionyl, butyryl, isobutyryl, valeryl, isovaleryl, pivaloyl, hexanoyl, trifluoroacetyl, in which preferable one is formyl or acetyl.

[0025] The aroyl may be substituted or unsubstituted one such as benzoyl, naphthoyl, toluoyl, di(tert-butyl)benzoyl, tolylbenzoyl, aminobenzoyl, tolylbenzoylaminobenzoyl.

[0026] The N-containing heterocyclic moiety in the term "an N-containing heterocycliccarbonyl" may be one containing at least one nitrogen atom mentioned above, in which preferable one is piperazinylcarbonyl, N-methylpiperazinylcarbonyl, N,N-dimethylpiperaziniocarbonyl, N-methylhomopiperazinylcarbonyl, N-(2-hydroxyethyl)piperazinylcarbonyl, N-(2-acetoxyethyl)piperazinylcarbonyl, N-(3-phthalimidopropyl)piperazinylcarbonyl, N-(3-aminopropyl)piperazinylcarbonyl, N-(pyrrolidinylcarbonylmethyl)piperazinylcarbonyl, N-(methylenedioxyphenylmethyl)piperazinylcarbonyl, N-ethoxycarbonylpiperazinylcarbonyl, N-carboxypiperazinylcarbonyl, and N-tert-butoxycarbonylpiperazinylcarbonyl.

[0027] The lower alkylsulfonyl may be methylsulfonyl, ethylsulfonyl, propylsulfonyl, butylsulfonyl and the like.

[0028] The arylsulfonyl may be substituted or unsubstituted one such as phenylsulfonyl, tolylsulfonyl, dimethoxyphenylsulfonyl, in which preferable one is dimethoxyphenylsulfonyl.

[0029] "N-Protective group" in "protected amino" may be common N-protective group such as substituted or unsubstituted lower alkanoyl [e.g. formyl, acetyl, propionyl, trifluoroacetyl, etc.], phthaloyl, lower alkoxycarbonyl [e.g. tert-butoxycarbonyl, tert-amyloxycarbonyl, etc.], substituted or unsubstituted aralkoxycarbonyl [e.g. benzyloxycarbonyl, p-nitrobenzyloxycarbonyl, etc.], substituted or unsubstituted arenesulfonyl [e.g. benzenesulfonyl, tosyl, etc.], nitrophenylsulfenyl, aralkyl [e.g. trityl, benzyl, etc.], in which preferable one is phthaloyl or tert-butoxycarbonyl.

[0030] "N-Protective group" in "N-protected piperazinylcarbonyl" may be common N-protective group such as substituted or unsubstituted lower alkanoyl [e.g. formyl, acetyl, propionyl, trifluoroacetyl, etc.], lower alkoxycarbonyl [e.g. tert-butoxycarbonyl, tert-amyloxycarbonyl, etc.], substituted or unsubstituted aralkoxycarbonyl [e.g. benzoloxycarbonyl, p-nitrobenzyloxycarbonyl, etc.], substituted or unsubstituted arenesulfonyl [e.g. benzenesulfonyl, tosyl, etc.], ni-

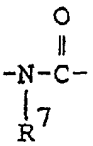
trophenylsulfenyl, aralkyl [e.g. trityl, benzyl, etc.], in which preferable one is tert-butoxycarbonyl.

[0031] "Protected hydroxy" may be commonly protected hydroxy such as substituted lower alkoxy such as lower alkoxy(lower)alkoxy [e.g. methoxymethoxy, etc.], lower alkoxy(lower)alkoxy(lower)alkoxy [e.g. methoxyethoxymethoxy, etc.], substituted or unsubstituted ar(lower)alkoxy [e.g. benzyloxy, nitrobenzyloxy, etc.], etc., acyloxy such as lower alkanoyloxy [e.g. acetoxy, propionyloxy, pivaloyloxy, etc.], aroyloxy [e.g. benzoyloxy, fluorenecarbonyloxy, etc.], lower alkoxycarbonyloxy [e.g. methoxycarbonyloxy, ethoxycarbonyloxy, propoxycarbonyloxy, isopropoxycarbonyloxy, butoxycarbonyloxy, isobutoxycarbonyloxy, tert-butoxycarbonyloxy, pentyloxycarbonyloxy, hexyloxycarbonyloxy, etc.], substituted or unsubstituted ar(lower)alkoxycarbonyloxy [e.g. benzyloxycarbonyloxy, bromobenzyloxycarbonyloxy, etc.] etc., tri(lower)alkylsilyloxy [e.g. trimethylsilyloxy, etc.].

[0032] Suitable "acid residue" may be halogen [e.g. fluoro, chloro, bromo, iodo], arenesulfonyloxy [e.g. benzenesulfonyloxy, tosyloxy, etc.], alkanesulfonyloxy [e.g. mesyloxy, ethanesulfonyloxy, etc.], in which preferable one is halogen.

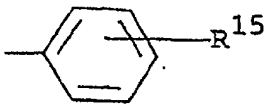
[0033] The phenyl group for R^{15} may be substituted with 1 to 5 substituent(s) as mentioned above, wherein the preferable number of the substituent(s) is 1 to 2.

[0034] Preferable compound (I) is one which has hydrogen for R^1, hydrogen, lower alkyl or halogen for R^2, hydrogen for R^3, hydrogen for R^4, hydrogen or lower alkoxy for R^5, hydrogen for R^6,



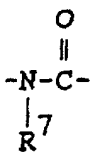
(wherein R^7 is lower alkyl optionally substituted with amino, lower alkylamino, protected amino, acyl or piperidino) or

(wherein R^{11} is hydrogen, lower alkylamino or acyl(lower)alkyl) for A, CH for X^1, CH for X^2,



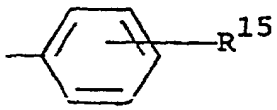
(wherein R^{15} is phenyl substituted with substituent(s) selected from the group consisting of lower alkyl, lower alkoxy, halogen, halo(lower)alkyl, hydroxy, amino(lower)alkyl, azido(lower)alkyl, lower alkylamino(lower)alkyl, acylamino(lower)alkyl, hydroxy(lower)alkyl, cyano and acyl) for Y, and 0, 1 or 2 for n.

[0035] More preferable compound (I) is one which has hydrogen for R^1, hydrogen, lower alkyl or halogen for R^2, hydrogen for R^3, hydrogen for R^4, hydrogen or lower alkoxy for R^5, hydrogen for R^6,



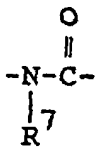
(wherein R^7 is lower alkyl substituted with N-lower alkylpiperazinylcarbonyl or lower alkyl substituted with di(lower) alkylamino) or

(wherein R^{11} is lower alkyl substituted with N-lower alkylpiperazinylcarbonyl) for A, CH for X^1, CH for X^2,

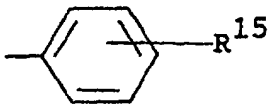


(wherein R^{15} is phenyl substituted with lower alkyl or di(lower alkyl)) for Y, and 0, 1 or 2 for n.

[0036] Most preferable compound (I) is one which has hydrogen for R^1, hydrogen for R^2, hydrogen for R^3, hydrogen for R^4, hydrogen for R^5, hydrogen for R^6,



(wherein R^7 is lower alkyl substituted with N-lower alkylpiperazinylcarbonyl)for A, CH for X^1, CH for X^2,



(wherein R^{15} is phenyl substituted with lower alkyl or di(lower alkyl)) for Y, and 1 for n.

[0037] Suitable pharmaceutically acceptable salts of the object compound (I) are conventional non-toxic salts and include an acid addition salt such as an inorganic acid addition salt [e.g. hydrochloride, hydrobromide, sulfate, phosphate, etc.], an organic acid addition salt [e.g. formate, acetate, trifluoroacetate, maleate, tartrate, methanesulfonate, benzenesulfonate, toluenesulfonate, etc.], a metal salt such as an alkali metal salt [e.g. sodium salt, potassium salt, etc.] and an alkaline earth metal salt [e.g. calcium salt, magnesium salt, etc.] and the like.

[0038] The processes for preparing the object compound (I) are explained in detail in the following.

Process 1

[0039] The object compound (Ia) or its salt can be prepared by reacting a compound (II) or its salt with a compound (III) or its reactive derivative at the carboxy group or a salt thereof.

[0040] Suitable salts of the compounds (Ia), (II) and (III) and its reactive derivative at the carboxy group may be the same as those exemplified for the compound (I).

[0041] Suitable reactive derivative at the carboxy group of the compound (III) may include an acid halide, an acid anhydride containing intramolecular, intermolecular and a mixed ones, an activated amide, an activated ester, and the like. Suitable examples of the reactive derivatives may be an acid chloride; an acid azide; a mixed acid anhydride with an acid such as substituted phosphoric acid [e.g. dialkylphosphoric acid, phenylphosphoric acid, diphenylphosphoric acid, dibenzylphosphoric acid, halogenated phosphoric acid, etc.], dialkylphosphorous acid, sulfurous acid, thiosulfuric acid, sulfuric acid, sulfonic acid [e.g. methanesulfonic acid, etc.], aliphatic carboxylic acid [e.g. acetic acid, propionic acid, butyric acid, isobutyric acid, pivalic acid, pentanoic acid, isopentanoic acid, 2-ethylbutyric acid, trichloroacetic acid, etc.] or aromatic carboxylic acid [e.g. benzoic acid, etc.]; a symmetrical acid anhydride; an activated amide with imidazole, 4-substituted imidazole, dimethylpyrazole, triazole or tetrazole; or an activated ester [e.g. cyanomethyl ester, methoxymethyl ester, dimethyliminomethyl [$(CH_3)_2\overset{+}{N}=CH$-] ester, vinyl ester, propargyl ester, p-nitrophenyl ester, 2,4-dinitrophenyl ester, trichlorophenyl ester, pentachlorophenyl ester, mesylphenyl ester, phenylazophenyl ester, phenyl thioester, p-nitrophenyl thioester, p-cresyl thioester, carboxymethyl thioester, pyranyl ester, pyridyl ester, piperidyl

ester, 8-quinolyl thioester, etc.] or an ester with an N-hydroxy compound [e.g. N,N-dimethylhydroxylamine, 1-hydroxy-2-(1H)-pyridone, N-hydroxysuccinimide, N-hydroxyphthalimide, 1-hydroxy-lH-benzotriazole, etc.] . These reactive derivatives can optionally be selected from them according to the kind of the compound (III) to be used.

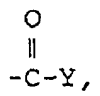
[0042] The reaction is usually carried out in a conventional solvent such as water, alcohol [e.g. methanol, ethanol, etc.], acetone, dioxane, acetonitrile, chloroform, methylene chloride, ethylene chloride, tetrahydrofuran, ethyl acetate, N,N-dimethylformamide, pyridine or any other organic solvent which does not adversely influence the reaction. These conventional solvents may also be used in a mixture with water.

[0043] In this reaction, when the compound (III) is used in a free acid form or its salt form, the reaction is preferably carried out in the presence of a conventional condensing agent such as N,N'-dicyclohexylcarbodiimide; N-cyclohexyl-N'-morpholinoethylcarbodiimide; N-cyclohexyl-N'-(4-diethylaminocyclohexyl)carbodiimide; N,N'-diethylcarbodiimide, N,N'-diisopropylcarbodiimide; N-ethyl-N'-(3-dimethylaminopropyl)carbodiimide; N,N'-carbonylbis-(2-methylimidazole); pentamethyleneketene-N-cyclohexylimine; diphenylketene-N-cyclohexylimine; ethoxyacetylene; 1-alkoxy-1-chloroethylene; trialkyl phosphite; ethyl polyphosphate; isopropyl polyphosphate; phosphorus oxychloride (phosphoryl chloride); phosphorus trichloride; diphenyl phosphorylazide; diphenyl chlorophosphate; diphenylphosphinic chloride; thionyl chloride; oxalyl chloride; lower alkyl haloformate [e.g. ethyl chloroformate, isopropyl chloroformate, etc.]; triphenylphosphine; 2-ethyl-7-hydroxybenzisoxazolium salt; 2-ethyl-5-(m-sulfophenyl)isoxazolium hydroxide intramolecular salt; 1-(p-chlorobenzenesulfonyloxy)-6-chloro-1H-benzotriazole; so-called Vilsmeier reagent prepared by the reaction of N,N-dimethylformamide with thionyl chloride, phosgene, trichloromethyl chloroformate, phosphorus oxychloride, etc..

[0044] The reaction may also be carried out in the presence of an inorganic or organic base such as an alkali metal bicarbonate, tri(lower)alkylamine, pyridine, 4-dimethylaminopyridine, N-(lower)alkylmorpholine, N,N-di(lower)alkylaniline (e.g. N,N-dimethylaniline, etc.) N,N-di(lower)alkylbenzylamine.

[0045] The reaction temperature is not critical, and the reaction is usually carried out under cooling to heating.

[0046] In this reaction, in case that the intramolecular acid anhydride (e.g. diphenic anhydride, etc.) is used as the reactive derivative at the carboxy group of the compound (III), the compound (Ia) having phenyl substituted with carboxy for R^{15} may be obtained. In case that the compound (II) having aminobenzoyl for R^7 in A used as a starting compound, the compound (Ia) having aminobenzoyl, amino in which is substituted with



for R^7 in A may be obtained. These cases are included within the scope of the present reaction.

Process 2

[0047] The object compound (Ic) or its salt can be prepared by reacting a compound (Ib) or its reactive derivative at the carboxy group or a salt thereof with an amine.

[0048] Suitable salts of the compounds (Ic) and (Ib) and its reactive derivative at the carboxy group may be the same as those exemplified for the compound (I).

[0049] Suitable "amine" may be ammonia optionally substituted with lower alkyl, lower alkylamino(lower)alkyl, a heterocyclic(lower)alkyl, acyl(lower)alkyl, lower alkylamino or a heterocyclic group, N-containing heterocyclic compound.

[0050] The ammonia substituted with lower alkyl, lower alkylamino(lower)alkyl, a heterocyclic(lower)alkyl, acyl(lower)alkyl, lower alkylamino or a heterocyclic group may be one substituted with those as illustrated above.

[0051] The N-containing heterocyclic compound may be saturated 5 to 7-membered N-, or N- and S-, or N- and O-containing heterocyclic compound such as pyrrolidine, imidazolidine, substituted or unsubstituted piperidine, substituted or unsubstituted piperazine, substituted or unsubstituted homopiperazine, morpholine, thiomorpholine, quinuclidine or the like, in which preferable one is piperazine, N-methylpiperazine, N-methylhomopiperazine, N-(2-hydroxyethyl)piperazine, N-(3-phthalimidopropyl)-piperazine, N-(2-acetoxyethyl)piperazine, N-(pyrrolidinylcarbonylmethyl)piperazine, N-(methylenedioxyphenylmethyl)piperazine, N-ethoxycarbonylpiperazine, N-carboxypiperazine, N-tert-butoxypiperazine, N-pyridylpiperazine or dimethylaminopiperidine.

[0052] This reaction can be carried out in substantially the same manner as Process 1, and therefore the reaction mode and reaction condition (e.g. solvent, reaction temperature, etc.) of this reaction are to be referred to those as explained in Process 1.

Process 3

[0053] The object compound (Ie) or its salt can be prepared by subjecting a compound (Id) or its salt to elimination reaction of the N-protective group.

[0054] Suitable salts of the compound (Id) and (Ie) may be the same as those exemplified for the compound (I).

[0055] This reaction is carried out in accordance with a conventional method such as hydrolysis, reduction or the like.

[0056] The hydrolysis is preferably carried out in the presence of a base or an acid including Lewis acid.

[0057] Suitable base may include an inorganic base and an organic base such as an alkali metal [e.g. sodium, potassium, etc.], an alkaline earth metal [e.g. magnesium, calcium, etc.], the hydroxide or carbonate or bicarbonate thereof, hydrazine, trialkylamine [e.g. trimethylamine, triethylamine, etc.], picoline, 1,5-diazabicyclo[4.3.0]-non-5-ene, 1,4-diazabicyclo[2.2.2]octane, 1,8-diazabicyclo[5.4.0]undec-7-ene.

[0058] Suitable acid may include an organic acid [e.g. formic acid, acetic acid, propionic acid, trichloroacetic acid, trifluoroacetic acid, etc.], an inorganic acid [e.g. hydrochloric acid, hydrobromic acid, sulfuric acid, hydrogen chloride, hydrogen bromide, hydrogen fluoride, etc.] and an acid addition salt compound [e.g. pyridine hydrochloride, etc.].

[0059] The elimination using trihaloacetic acid [e.g. trichloroacetic acid, trifluoroacetic acid, etc.] or the like is preferably carried out in the presence of cation trapping agents [e.g. anisole, phenol, etc.].

[0060] The reaction is usually carried out in a solvent such as water, an alcohol [e.g. methanol, ethanol, etc.], methylene chloride, chloroform, tetrachloromethane, tetrahydrofuran, a mixture thereof or any other solvent which does not adversely influence the reaction. A liquid base or acid can be also used as the solvent. The reaction temperature is not critical and the reaction is usually carried out under cooling to heating.

[0061] The reduction method applicable for the elimination reaction may include chemical reduction and catalytic reduction.

[0062] Suitable reducing agents to be used in chemical reduction are a combination of metal [e.g. tin, zinc, iron, etc.] or metallic compound [e.g. chromium chloride, chromium acetate, etc.] and an organic or inorganic acid [e.g. formic acid, acetic acid, propionic acid, trifluoroacetic acid, p-toluenesulfonic acid, hydrochloric acid, hydrobromic acid, etc.].

[0063] Suitable catalysts to be used in catalytic reduction are conventional ones such as platinum catalysts [e.g. platinum plate, spongy platinum, platinum black, colloidal platinum, platinum oxide, platinum wire, etc.], palladium catalysts [e.g. spongy palladium, palladium black, palladium oxide, palladium on carbon, colloidal palladium, palladium on barium sulfate, palladium on barium carbonate, etc.], nickel catalysts [e.g. reduced nickel, nickel oxide, Raney nickel, etc.], cobalt catalysts [e.g. reduced cobalt, Raney cobalt, etc.], iron catalysts [e.g. reduced iron, Raney iron, etc.], copper catalysts [e.g. reduced copper, Raney copper, Ullman copper, etc.].

[0064] In case that the N-protective group is benzyl, the reduction is preferably carried out in the presence of a combination of palladium catalysts [e.g. palladium black, pallaidum on carbon, etc.] and formic acid or its salt [e.g. ammonium formate, etc.].

[0065] The reduction is usually carried out in a conventional solvent which does not adversely influence the reaction such as water, methanol, ethanol, propanol, N,N-dimethylformamide, or a mixture thereof. Additionally, in case that the above-mentioned acids to be used in chemical reduction are in liquid, they can also be used as a solvent. Further, a suitable solvent to be used in catalytic reduction may be the above-mentioned solvent, and other conventional solvent such as diethyl ether, dioxane, tetrahydrofuran, etc. or a mixture thereof.

[0066] The reaction temperature of this reduction is not critical and the reaction is usually carried out under cooling to heating.

Process 4

[0067] The object compound (Ig) or its salt can be prepared by subjecting a compound (If) or its salt to reduction.

[0068] Suitable salts of the compounds (If) and (Ig) may be the same as those exemplified for the compound (I).

[0069] The reduction may include chemical reduction and catalytic reduction, which are carried out in a conventional manner.

[0070] Suitable reducing agents to be used in chemical reduction are a metal [e.g. tin, zinc, iron, etc.], a combination of such metal and/or metallic compound [e.g. chromium chloride, chromium acetate, etc.] and an organic or inorganic acid [e.g. formic acid, acetic acid, propionic acid, trifluoroacetic acid, p-toluenesulfonic acid, hydrochloric acid, hydrobromic acid, etc.], a combination of such metal and/or metallic compound and base [e.g. ammonia, ammonium chloride, sodium hydroxide, etc.], a metal hydride compound such as aluminum hydride compound [e.g. lithium aluminum hydride, sodium aluminum hydride, aluminum hydride, lithium trimethoxyaluminum hydride, lithium tri-t-butoxyaluminum hydride, etc.], borohydride compound [e.g. sodium borohydride, lithium borohydride, sodium cyanoborohydride, tetramethylammonium borohydride, bonane, diborane, etc.], a phosphorus compound [e.g. phosphorus trichloride, phosphorus tribromide, triphenylphosphine, triethylphosphine, etc.].

[0071] Suitable catalysts to be used in catalytic reduction are conventional ones such as platinum catalyst [e.g.

platinum plate, spongy platinum, platinum black, colloidal platinum, platinum oxide, platinum wire, etc.], palladium catalyst [e.g. spongy palladium, palladium black, palladium oxide, palladium on carbon, colloidal palladium, palladium on barium sulfate, palladium on barium carbonate, etc.], nickel catalyst [e.g. reduced nickel, nickel oxide, Raney nickel, etc.], cobalt catalyst [e.g. reduced cobalt, Raney cobalt, etc.], iron catalyst [e.g. reduced iron, Raney iron, etc.], copper catalyst [e.g. reduced copper, Raney copper, Ullman copper, etc.].

[0072] The reduction is usually carried out in a solvent. A suitable solvent to be used may be water, an alcohol [e.g. methanol, ethanol, propanol, etc.], acetonitrile or any other conventional organic solvent such as diethyl ether, dioxane, tetrahydrofuran, etc. or a mixture thereof.

[0073] The reaction temperature is not critical, and the reaction is preferably carried out under cooling to heating.

Process 5

[0074] The object compound (Ih) or its salt can be prepared by reacting a compound (Ig) or its salt with an acylating agent.

[0075] Suitable salt of the compound (Ig) may be the same as those exemplified for the compound (I).

[0076] Suitable salt of the compound (Ih) may be an acid addition salt as those exemplified for the compound (I).

[0077] The acylating agent may include an organic acid represented by the formula : R^{17}-OH, in which R^{17} is acyl as illustrated above, or its reactive derivative.

[0078] The suitable reactive derivative of organic acid may be a conventional one such as an acid halide [e.g. acid chloride, acid bromide, etc.], an acid azide, an acid anhydride, an activated amide, an activated ester.

[0079] When free acid is used as an acylating agent, the acylation reaction may preferably be conducted in the presence of a conventional condensing agent such as N,N'-dicyclohexylcarbodiimide.

[0080] The reaction is usually carried out in a conventional solvent such as water, acetone, dioxane, chloroform, methylene chloride, acetonitrile, ethylene chloride, tetrahydrofuran, ethyl acetate, N,N-dimethylformamide, pyridine or any other organic solvent which does not adversely influence the reaction, or a mixture thereof.

[0081] The reaction is also preferably carried out in the presence of a conventional base such as triethylamine, pyridine, sodium hydroxide.

[0082] The reaction temperature is not critical, and the reaction can be carried out under cooling to heating.

Process 6

[0083] The object compound (Ii) or its salt can be prepared by reacting a compound (Ig) or its salt with an alkylating agent.

[0084] Suitable salts of the compounds (Ig) and (Ii) may be the same as those exemplified for the compound (I).

[0085] Suitable alkylating agent may be lower alkyl halide [e.g. methyl iodide, ethyl bromide, etc.], a combination of a carbonyl compound such as aliphatic ketone [e.g. acetone, ethyl methyl ketone, etc.], carbaldehyde [e.g. formaldehyde, ethanal, etc.], orthocarboxylic acid ester [e.g. triethyl orthoformate, etc.], and a reducing agent including chemical and catalytic ones [e.g. formic acid, sodium borohydride, sodium cyanoborohydride, palladium on carbon, etc.].

[0086] When lower alkyl halide is used as alkylating agent, the reaction is preferably carried out in the presence of a base such as an alkali metal [e.g. sodium, potassium, etc.], an alkaline earth metal [e.g. magnesium, calcium, etc.], the hydride or hydroxide or carbonate or bicarbonate thereof, tri(lower)alkylamine, N,N-di(lower)-alkylaniline.

[0087] The reaction is usually carried out in a conventional solvent which does not adversely influence the reaction such as water, dioxane, an alcohol [e.g. methanol, ethanol, etc.], acetonitrile, tetrahydrofuran, acetic acid, N,N-dimethylformamide, or a mixture thereof.

[0088] Additionally, in case that the above-mentioned alkylating agent or base is in liquid, it can also be used as a solvent.

[0089] The reaction temperature is not critical and the reaction can be carried out under cooling to heating.

[0090] In this reaction, in case that the compound (Ig) having lower alkyl substituted with amino for R^7 in A is used as a starting compound, the compound (Ii) having lower alkyl substituted with lower alkylamino for R^7 in A may be obtained according to reaction conditions. This case is included within the scope of the present reaction.

Process 7

[0091] The object compound (Ik) or its salt can be prepared by reacting a compound (Ij) or its salt with an alkylating agent.

[0092] Suitable salts of the compounds (Ij) and (Ik) may be the same as those exemplified for the compound (I).

[0093] This reaction can be carried out in substantially the same manner as that of Process 6, and therefore the reaction mode and reaction condition (e.g. solvent, reaction temperature, etc.) of this reaction are to be referred to

those as explained in Process 6.

[0094] In this reaction, in case that the compound (Ij) having phenyl substituted with amino(lower)alkyl for R^{15} in Y is used as a starting compound, the compound (Ik) having phenyl substituted with lower alkylamino(lower)alkyl for R^{15} in Y may be obtained according to reaction condition. This case is included within the scope of the present reaction.

Process 8

[0095] The object compound (Im) or its salt can be prepared by subjecting a compound (Iℓ) or its salt to dealkylation reaction.

[0096] Suitable salts of the compounds (Iℓ) and (Im) may be the same as those exemplified for the compound (I).

[0097] The reaction is carried out in accordance with a conventional method such as hydrolysis.

[0098] The hydrolysis is preferably carried out in the presence of an acid including Lewis acid [e.g. hydrochloric acid, hydrobromic acid, hydroiodic acid, boron tribromide, boron trichloride, etc.] or tri(lower)alkyl silyliodide [e.g. trimethylsilyliodide, etc.].

[0099] The reaction is usually carried out in a solvent such as water, acetic acid, methylene chloride, tetrahydrofuran, a mixture thereof or any other solvent which does not adversely influence the reaction.

[0100] The reaction temperature is not critical and the reaction is usually carried out under cooling to heating.

Process 9

[0101] The object compound (Io) or its salt can be prepared by subjecting a compound (In) or its salt to deesterification reaction.

[0102] Suitable salts of the compounds (In) and (Io) may be the same as those exemplified for the compound (I).

[0103] The reaction is carried out in accordance with a conventional method such as hydrolysis, reduction or the like.

[0104] The hydrolysis is preferably carried out in the present of a base or an acid including Lewis acid. Suitable base may include an inorganic base and an organic base such as an alkali metal [e.g. lithium, sodium, potassium, etc.], an alkaline earth metal [e.g. magnesium, calcium, etc.], the hydroxide or carbonate or bicarbonate thereof, trialkylamine [e.g. trimethylamine, triethylamine, etc.], picoline, 1,5-diazabicyclo[4.3.0]-non-5-ene, 1,4-diazabicyclo[2.2.2]octane, 1,8-diazabicyclo[5.4.0]undec-7-ene. Suitable acid may include an organic acid [e.g. formic acid, acetic acid, propionic acid, trichloroacetic acid, trifluoroacetic acid, etc.], an inorganic acid [e.g. hydrochloric acid, hydrobromic acid, hydroiodic acid, sulfuric acid, etc.] and Lewis acid [e.g. boron tribromide, etc.].

[0105] The reaction is usually carried out in a solvent such as water, an alcohol [e.g. methanol, ethanol, etc.], xylene, diethylene glycol monomethyl ethyl, methylene chloride, tetrahydrofuran, a mixture thereof or any other solvent which does not adversely influence the reaction. A liquid base or acid can be also used as the solvent. The reaction temperature is not critical and the reaction is usually carried out under cooling to warming.

[0106] The reduction can be applied preferably for elimination of the ester moiety such as 4-nitrobenzyl, 2-iodoethyl, 2,2,2-trichloroethyl). The reduction method applicable for the elimination reaction may include chemical reduction and catalitic reduction.

[0107] Suitable reducing agents to be used in chemical reduction are a combination of metal [e.g. tin, zinc, iron, etc.] or metallic compound [e.g. chromium chloride, chromium acetate, etc.] and an organic or inorganic acid [e.g. formic acid, acetic acid, propionic acid, trifluoroacetic acid, p-toluenesulfonic acid, hydrochloric acid, hydrobromic acid, etc.].

[0108] Suitable catalysts to be used in catalytic reduction are conventional ones such as platinum catalysts [e.g. platinum plate, spongy platinum, platinum black, colloidal platinum, platinum oxide, platinum wire, etc.], palladium catalyst [e.g. spongy palladium, pallaidum black, palladium oxide, palladium on carbon, colloidal palladium, palladium on barium sulfate, palladium on barium carbonate, etc.], nickel catalyst [e.g. reduced nickel, nickel oxide, Raney nickel, etc.], cobalt catalyst [e.g. reduced cobalt, Raney cobalt, etc.], iron catalyst [e.g. reduced iron, Raney iron, etc.], copper catalyst [e.g. reduced copper, Raney copper, Ullman copper, etc.].

[0109] The reduction is usually carried out in a conventional solvent which does not adversely influence the reaction such as water, an alcohol [e.g. methanol, ethanol, propanol, etc.], N,N-dimethylformamide, or a mixture thereof. Additionally, in case that the above-mentioned acids to be used in chemical reduction are in liquid, they can also be used as a solvent. Further, a suitable solvent to be used in catalytic reduction may be the above-mentioned solvent, and other conventional solvent such as diethyl ether, dioxane, tetrahydrofuran, etc., or a mixture thereof.

[0110] The reaction temperature of this reduction is not critical and the reaction is usually carried out under cooling to warming.

Process 10

[0111] The object compound (Iq) or its salt can be prepared by reacting a compound (Ip) or its reactive derivative at

the carboxy group or a salt thereof with a hydroxy compound.

[0112] Suitable salts of the compounds (Iq) and (Ip) and its reactive derivative at the carboxy group may be the same as those exemplified for the compound (I).

[0113] Suitable reactive derivative at the carboxy group of the compound (Ip) may be acid halide [e.g. acid chloride, acid bromide, etc.].

[0114] Suitable hydroxy compound may be an alcohol [e.g. methanol, ethanol, propanol, benzyl alcohol, 2-dimethylaminoethanol, etc.], phenol, naphthol.

[0115] The reaction is usually carried out in a conventional solvent such as diethyl ether, tetrahydrofuran, dioxane, methylene chloride or any other organic solvent which does not adversely influence the reaction.

[0116] Additionally, in case that the above-mentioned hydroxy compound is in liquid, it can also be used as a solvent.

[0117] The reaction temperature is not critical and the reaction is usually carried out under cooling to heating.

[0118] When the compound (Ip) is used in a free acid form in the reaction, the reaction is preferably carried out in the presence of an acid or a conventional condensing agent as illustrated in Process 1.

[0119] Suitable acid may be an organic acid [e.g. formic acid, acetic acid, propionic acid, trifluoroacetic acid, trichloroacetic acid, etc.], an inorganic acid [e.g. hydrogen chloride, hydrochloric acid, hydrobromic acid, hydroiodic acid, sulfuric acid, etc.] and Lewis acid [e.g. boron tribromide, etc.].

[0120] In this reaction, in case that the reaction is carried out in the presence of a condensing agent, the reaction mode and reaction condition (e.g. solvent, reaction temperature) of this reaction are to be referred to those as explained in Process 1.

Process 11

[0121] The object compound (Is) or its salt can be prepared by reacting a compound (Ir) or its salt with a reducing agent.

[0122] Suitable salts of the compounds (Ir) and (Is) may be the same as those exemplified for the compound (I).

[0123] Suitable reducing agent may *be* diborane, lithium aluminum hydride.

[0124] The reaction is usually carried out in a conventional solvent such as diethyl ether, tetrahydrofuran or any other organic solvent which does not adversely influence the reaction.

[0125] The reaction temperature is not critical, and the reaction can be carried out under cooling to heating.

Process 12

[0126] The object compound (In) or its salt can be prepared by reacting a compound (Io) or its reactive derivative at the carboxy group or a salt thereof with a hydroxy compound.

[0127] Suitable salts of the compound (In) and (Io) and its reactive derivative at the carboxy group may be the same as those exemplified for the compound (I).

[0128] Suitable reactive derivative at the carboxy group of the compound (Io) may be acid halide [e.g. acid chloride, acid bromide, etc.].

[0129] This reaction can be carried out in substantially the same manner as that of Process 10, and therefore the reaction mode and reaction condition (e.g. solvent, reaction temperature, etc.) of this reaction are to be referred to those as explained in Process 10.

Process 13

[0130] The object compound (I) or its salt can be prepared by reacting a compound (IV) or its salt with a compound (V) or its reactive derivatives at the carboxy group or a salt thereof.

[0131] Suitable salts of the compounds (IV) and (V) and its reactive derivative at the carboxy group may be the same as those exemplified for the compound (I).

[0132] This reaction can be carried out in substantially the same manner as Process 1, and therefore the reaction mode and reaction condition (e.g. solvent, reaction temperature, etc.) of this reaction are to be referred to those as explained in Process 1.

Process 14

[0133] The object compound (Iu) or its salt can be prepared by subjecting a compound (It) or its salt to elimination reaction of hydroxy protective group.

[0134] Suitable salts of the compounds (It) and (Iu) may be the same as those exemplified for the compound (I).

[0135] This reaction is carried out in accordance with a conventional method such as hydrolysis.

[0136] The hydrolysis is preferably carried out in the present of a base or an acid including Lewis acid. Suitable base may include an inorganic base and an organic base such as an alkali metal [e.g. lithium, sodium, potassium, etc.], an alkaline earth metal [e.g. magnesium, calcium, etc.], the hydroxide or carbonate or bicarbonate thereof, trialkylamine [e.g. trimethylamine, triethylamine, etc.], picoline, 1,5-diazabicyclo[4.3.0]-non-5-ene, 1,4-diazabicyclo[2.2.2]octane, 1,8-diazabicyclo[5.4.0]undec-7-ene. Suitable acid may include an organic acid [e.g. formic acid, acetic acid, propionic acid, trichloroacetic acid, trifluoroacetic acid, etc.], an inorganic acid [e.g. hydrochloric acid, hydrobromic acid, hydroiodic acid, sulfuric acid, etc.] and Lewis acid [e.g. boron tribromide, etc.].

[0137] The reaction is usually carried out in a solvent such as water, an alcohol [e.g. methanol, ethanol, etc.], xylene, diethylene glycol monomethyl ethyl, methylene chloride, tetrahydrofuran, a mixture thereof or any other solvent which does not adversely influence the reaction. A liquid base or acid can be also used as the solvent. The reaction temperature is not critical and the reaction is usually carried out under cooling to warming.

Process 15

[0138] The object compound (Ix) or its salt can be prepared by reacting a compound (Iu) or its salt with an oxidizing agent.

[0139] Suitable salts of the compounds (Iu) and (Ix) may be the same as those exemplified for the compound (I).

[0140] Suitable oxidizing agent may be dimethyl sulfoxide, a mixture of dimethyl sulfoxide and oxalyl chloride.

[0141] This reaction is preferably carried out in the presence of alkali metal iodide [e.g. sodium iodide, etc.] and alkali metal carbonate [e.g. sodium carbonate] or tri(lower)alkylamine [e.g. triethylamine, etc.].

[0142] The reaction is usually carried out in a solvent which does not adversely influence the reaction such as dimethoxyethane, dichloromethane. Additionally in case that the above-mentioned oxidizing agent is in liquid, it can also be used as a solvent.

[0143] The reaction temperature is not critical and the reaction is carried out under cooling to heating.

Process 16

[0144] The object compound (Iy) or its salt can be prepared by reacting a compound (Ix) or its salt with di(lower) alkylamine or N-containing heterocyclic compound in the presence of a reducing agent.

[0145] Suitable salts of the compounds (Ix) and (Iy) may be the same as those exemplified for the compound (I).

[0146] Suitable di(lower)alkylamine, lower alkyl in which may be the same and different, may be dimethylamine, diethylamine, N-methyl-N-ethylamine.

[0147] Suitable N-containing heterocyclic compound may be one as exemplified in Process 3.

[0148] Suitable reducing agent may include chemical and catalytic one [e.g. formic acid, sodium borohydride, sodium cyanoborohydride, palladium on carbon, etc.].

[0149] The reaction is usually carried out in a conventional solvent which does not adversely influence the reaction such as water, dioxane, an alcohol [e.g. methanol, ethanol, etc.], acetonitrile, tetrahydrofuran, acetic acid, N,N-dimethylformamide, or a mixture thereof.

[0150] The reaction temperature is not critical and the reaction can be carried out under cooling to heating.

Process 17

[0151] The object compound (I-1) or its salt can be prepared by subjecting a compound (Iz) or its salt to acylation reaction.

[0152] Suitable salts of the compounds (Iz) and (I-1) may be the same as those exemplified for the compound (I).

[0153] This reaction can be carried out in substantially the same manner as Process 5, and therefore the reaction mode and reaction condition (e.g. solvent, reaction temperature, etc.) of this reaction are to be referred to those as explained in Process 5.

Process 18

[0154] The object compound (I-5) or its salt can be prepared by reacting a compound (I-4) or its salt with lower alkyl halide or its salt, lower alkyl in which may be substituted with lower alkylamino, in the presence of a base.

[0155] Suitable salts of the compounds (I-4) and (I-5) may be the same as those exemplified for the compound (I).

[0156] Suitable salt of lower alkyl halide, lower alkyl in which is substituted with lower alkylamino may be an acid addition salt as exemplified for the compound (I).

[0157] Suitable base may be alkali metal [e.g. lithium, sodium, potassium, etc.], the hydroxide or carbonate or bicarbonate thereof [e.g. sodium hydroxide, potassium carbonate, potassium bicarbonate, etc.], alkaline earth metal [e.g.

calcium, magnesium, etc.], alkali metal hydride [e.g. sodium hydride, etc.], alkaline earth metal hydride [e.g. calcium hydride, etc.], alkali metal alkoxide [e.g. sodium methoxide, sodium ethoxide, potassium tert-butoxide, etc.], alkaline earth metal alkoxide [e.g. magnesium methoxide, magnesium ethoxide, etc.].

[0158] The reaction is also preferably carried out in the presence of alkali metal iodide [e.g. sodium iodide, potassium iodide, etc.].

[0159] This reaction is usually carried out in a conventional solvent such as tetrahydrofuran, dioxane, aromatic hydrocarbon [e.g. benzene, toluene, xylene, etc.], N,N-dimethylformamide, acetone, a mixture thereof, or any other solvent which does not adversely influence the reaction.

[0160] The reaction temperature is not critical, and the reaction is usually carried out under cooling to heating.

Process 19

[0161] The object compound (I-6) or its salt can be prepared by reacting a compound (Ia) or its salt with an alkylating or acylating agent.

[0162] Suitable salts of the compounds (Ia) and (I-6) may be the same as those exemplified for the compound (I).

[0163] Suitable alkylating agent may be lower alkyl halide [e.g. methyl iodide, ethyl bromide, etc.].

[0164] Suitable acylating agent may be a reactive derivative of organic acid as illustrated in Process 5.

[0165] The reaction is preferably carried out in the presence of a base such as an alkali metal [e.g. sodium, potassium, etc.], an alkaline earth metal [e.g. magnesium, calcium, etc.], the hydride or hydroxide or carbonate or bicarbonate thereof, tri(lower)alkylamine, N,N-di(lower)alkylaniline, 4-di(lower)alkylaminopyridine [e.g. 4-dimethylaminopyridine, etc.].

[0166] The reaction is usually carried out in a conventional solvent such as acetone, dioxane, chloroform, methylene chloride, acetonitrile, ethylene chloride, tetrahydrofuran, ethyl acetate, N,N-dimethylformamide, pyridine or any other organic solvent which does not adversely influence the reaction, or a mixture thereof.

[0167] The reaction temperature is not critical, and the reaction is preferably carried out under cooling to heating.

Process 20

[0168] The object compound (I-8) or its salt can be prepared by reacting a compound (I-7) or its salt with lower alkyl halide.

[0169] Suitable salt of the compound (I-7) may be an acid addition salt as exemplified for the compound (I).

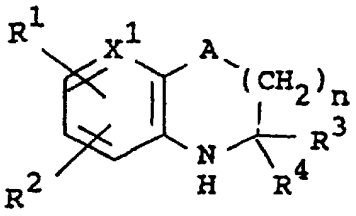
[0170] Suitable salt of the compound (I-8) may be halide.

[0171] The reaction is usually carried out in a conventional solvent such as acetone, dioxane, chloroform, methylene chloride, acetonitrile, tetrahydrofuran or any other organic solvent which does not adversely influence the reaction, or a mixture thereof.

[0172] The reaction temperature is not critical, and the reaction is preferably carried out under cooling to heating.

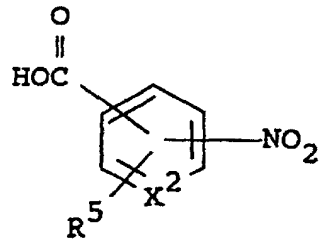
[0173] The starting compounds (II), (IIa), (IVa), (IVb), (IVc) and (V) or a salt thereof can be prepared by the following processes.

Process A

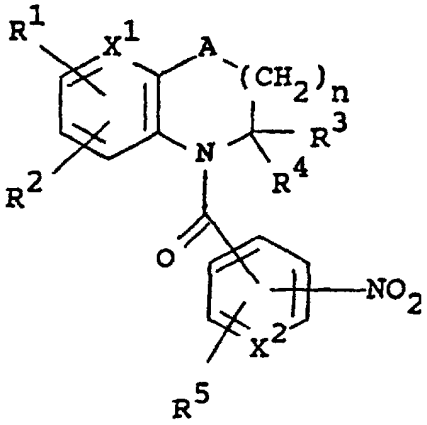


(IV)
or its salt

+

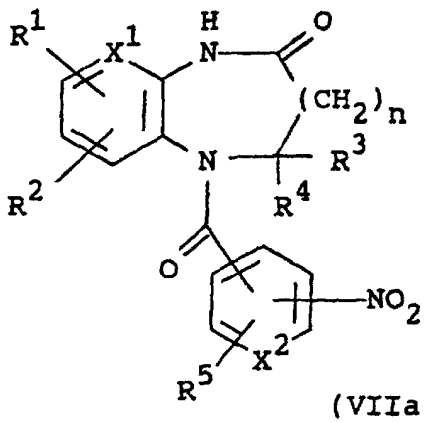


(VI)
or its reactive derivative at the carboxy group or a salt thereof



(VII)
or its salt

Process B



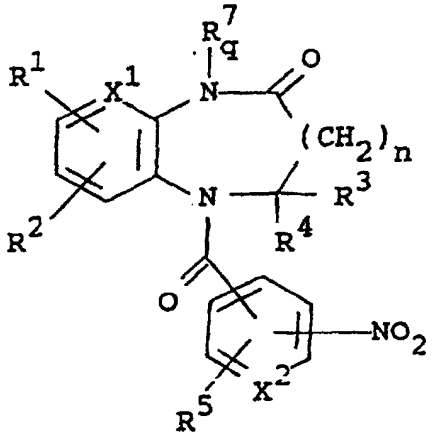
(VIIa)

or its salt

$Z^1-R^7_q$

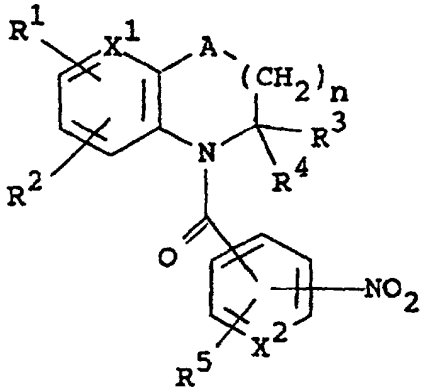
(VIII)

or its salt



(VIIb)

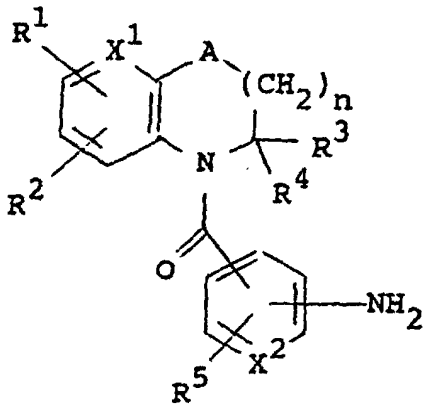
Process C



(VII)

or its salt

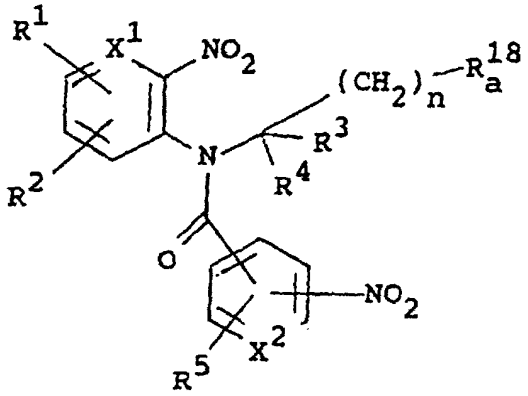
reduction



(II)

or its salt

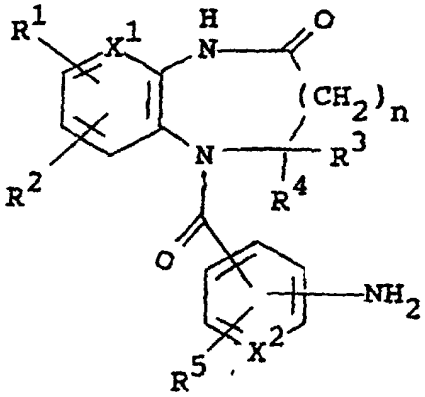
Process D



reduction

(IX)

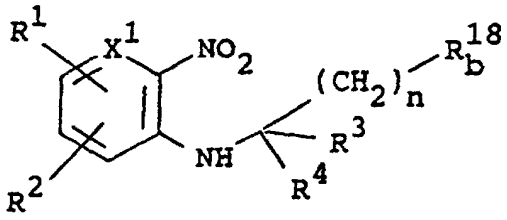
or its salt



(IIa)

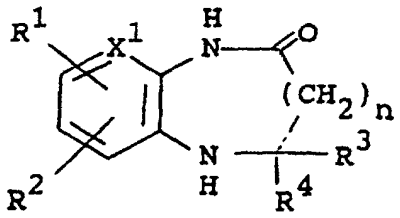
or its salt

Process E



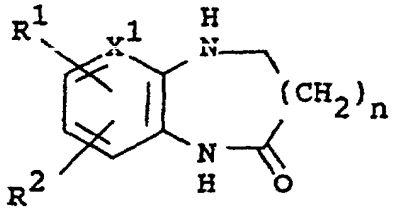
reduction

(X)
or its salt



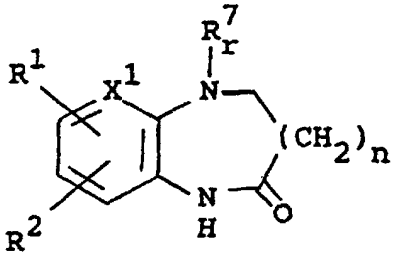
(IVa)
or its salt

Process F



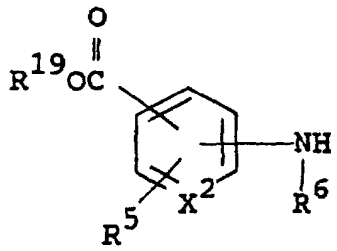
acylation

(IVb)
or its salt



(IVc)
or its salt

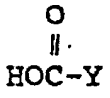
Process G



(XI)

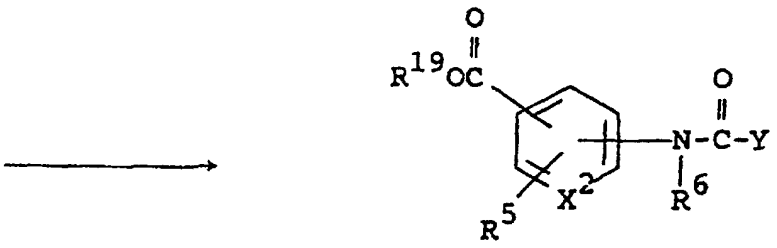
or its salt

+



(XII)

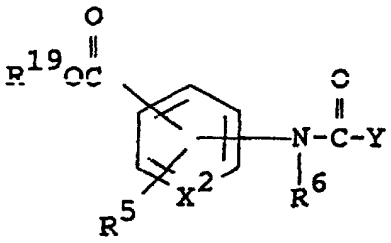
or its reactive derivative at the carboxy group or a salt thereof



(XIII)

or its salt

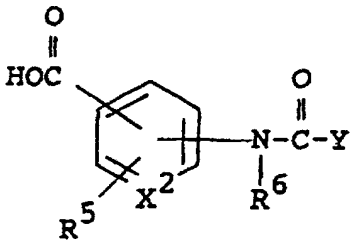
Process H



(XIII)

or its salt

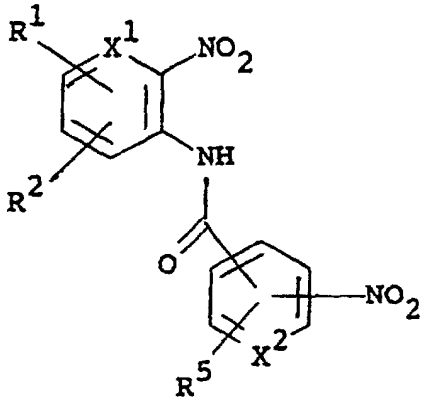
deesterification



(V)

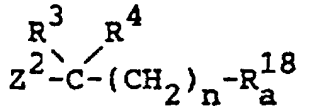
or its salt

Process I



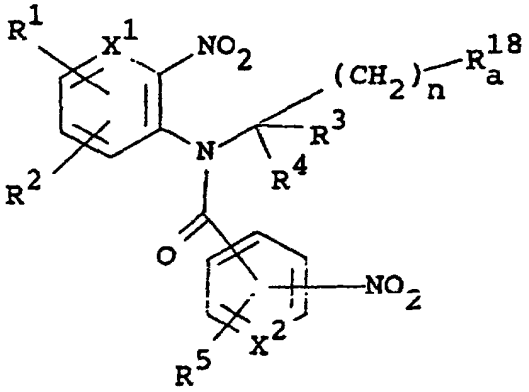
(XIV)

or its salt



(XV)

or its salt



(IX)

or its salt

wherein

R^1, R^2, R^3, R^4, R^5, R^6, A, X^1, X^2, Y and n	are each as defined above,
R^7_q	is lower alkyl optionally substituted with halogen, amino, lower alkylamino, protected amino, acyl, a heterocyclic group, hydroxy or protected hydroxy,
Z^1	is acid residue,
R^{18}	is carboxy or esterified carboxy,
R^{18a}	is carboxy or esterified carboxy,
R^{7b}	is acyl,
R^{19}	is esterified carboxy, and
Z^{2a}	is acid residue.

[0174] The above-mentioned processes for preparing the starting compounds are explained in detail in the following.

Process A

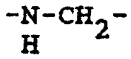
[0175] The compound (VII) or its salt can be prepared by reacting a compound (IV) or its salt with a compound (VI) or its reactive derivative at the carboxy group or a salt thereof.

[0176] Suitable salts of the compounds (IV) and (VII) may be the same as those exemplified for the compound (I).

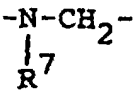
[0177] Suitable salts of the compound (VI) and its reactive derivative at the carboxy group may be a base salt as exemplified for the compound (I).

[0178] This reaction can be carried out in substantially the same manner as Process 1, and therefore the reaction mode and reaction condition (e.g. solvent, reaction temperature, etc.) of this reaction are to be referred to those as explained in Process 1.

[0179] In this reaction, in case that the compound (IV) having



for A and nitrobenzoic acid as the compound (VI) are used as a starting compound, the compound having



(wherein R^7 is nitrobenzoyl) for A may be obtained according to reaction conditions. This case is included within the scope of the present reaction.

Process B

[0180] The compound (VIIb) or its salt can be prepared by reacting a compound (VIIa) or its salt with a compound (VIII) or its salt.

[0181] Suitable salt of the compound (VIIa) may be an acid addition salt as exemplified for the compound (I).

[0182] Suitable salts of the compounds (VIIb) and (VIII) may be the same as those exemplified for the compound (I).

[0183] This reaction can be carried out in substantially the same manner as Process 6, and therefore the reaction mode and reaction condition (e.g. solvent, reaction temperature, etc.) of this reaction are to be referred to those as explained in Process 6.

[0184] In this reaction, in case that the compound (VIII) having lower alkyl substituted with acyl for R^7_q and chlorine for Z^1 [e.g. methyl chloroacetate, etc.] is used as a starting compound, the reaction is preferably carried out in the presence of an alkali metal iodide [e.g. sodium iodide, potassium iodide, etc.].

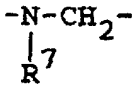
Process C

[0185] The compound (II) or its salt can be prepared by subjecting a compound (VII) or its salt to reduction.

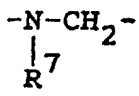
[0186] suitable salts of the compounds (II) and (VII) may be the same as those exemplified for the compound (I).

[0187] This reaction can be carried out in substantially the same manner as Process 4, and therefore the reaction mode and reaction condition (e.g. solvent, reaction temperature, etc.) of this reaction are to be referred to those as explained in Process 4.

[0188] In this reaction, in case that the compound (VII) having



(wherein R^7 is nitrobenzoyl) for A is used as a starting compound, the compound (II) having



(wherein R^7 is aminobenzoyl) for A may be obtained according to reaction conditions. This case is included within the scope of the present reaction.

[0189] In this reaction, in case that the compound (VII) having protected hydroxy for R^5 is used as a starting compound, the compound (II) having hydroxy for R^5 may be obtained according to reaction conditions. This case is included within the scope of the present reaction.

Process D

[0190] The compound (IIa) or its salt can be prepared by subjecting a compound (XI) or its salt to reduction.

[0191] Suitable salt of the compound (IIa) may be an acid addition salt as exemplified for the compound (I).

[0192] Suitable salt of the compound (IX) may be a base salt as exemplified for the compound (I).

[0193] This reaction can be carried out in substantially the same manner as Process 4, and therefore the reaction mode and reaction condition (e.g. solvent, reaction temperature, etc.) of this reaction are to be referred to those as explained in Process 4.

Process E

[0194] The compound (IVa) or its salt can be prepared by subjecting a compound (X) or its salt to reduction.

[0195] Suitable salt of the compound (IVa) may be an acid addition salt as exemplified for the compound (I).

[0196] Suitable salt of the compound (X) may be the same as those exemplified for the compound (I).

[0197] This reaction can be carried out in substantially the same manner as Process 4, and therefore the reaction mode and reaction condition (e.g. solvent, reaction temperature, etc.) of this reaction are to be referred to those as explained in Process 4.

Process F

[0198] The compound (IVc) or its salt can be prepared by reacting a compound (IVb) or its salt with an acylating agent.

[0199] Suitable salts of the compounds (IVb) and (IVc) may be acid addition salts as exemplified for the compound (I).

[0200] This reaction can be carried out in substantially the same manner as Process 5, and therefore the reaction mode and reaction condition (e.g. solvent, reaction temperature, etc.) of this reaction are to be referred to those as explained in Process 5.

Process G

[0201] The compound (XIII) or its salt can be prepared by reacting a compound (XI) or its salt with a compound (XII) or its reactive derivative at the carboxy group or a salt thereof.

[0202] Suitable salt of the compound (XI) may be an acid addition salt as exemplified for the compound (I).

[0203] Suitable salts of the compounds (XIII) and (XII) and its reactive derivative at the carboxy group may be the same as those exemplified for the compound (I).

[0204] This reaction can be carried out in substantially the same manner as Process 1, and therefore the reaction mode and reaction condition (e.g. solvent, reaction temperature, etc.) of this reaction are to be referred to those as explained in Process 1.

[0205] In this reaction, in case that the compound (XI) having hydrogen for R^6 and the compound (XII) having tolylphenyl for Y are used as a starting compound, the compound (XIII) having tolylbenzoyl for R^6 may be obtained according to reaction conditions. This case is included within the scope of this reaction.

Process H

[0206] The compound (V) or its salt can be prepared by subjecting a compound (XIII) or its salt to deesterification reaction.

[0207] Suitable salts of the compounds (V) and (XIII) may be the same as those exemplified for the compound (I).

[0208] This reaction can be carried out in substantially the same manner as Process 9, and therefore the reaction mode and reaction condition (e.g. solvent, reaction temperature, etc.) of this reaction are to be referred to those as

explained in Process 9.

[0209] In this reaction, in case that the compound (XIII) having acyl for R^6 is used as a starting compound, the compound (V) having hydrogen for R^6 may be obtained according to reaction conditions. This case is included the scope of the present reaction.

Process I

[0210] The compound (IX) or its salt can be prepared by reacting a compound (XIV) or its salt with a compound (XV) or its salt.

[0211] Suitable salt of the compound (XIV) may be an acid addition salt as exemplified for the compound (I).

[0212] Suitable salt of the compound (XV) may be a base salt as exemplified for the compound (I).

[0213] Suitable salt of the compound (IX) may be the same as those exemplified for the compound (I).

[0214] This reaction can be carried out in substantially the same manner as Process 6, and therefore the reaction mode and reaction condition (e.g. solvent, reaction temperature, etc.) of this reaction are to be referred to those as explained in Process 6.

[0215] The compounds obtained by the above processes can be isolated and purified by a conventional method such as pulverization, recrystallization, column chromatography, reprecipitation, and converted to desired salt in conventional manner, if necessary.

[0216] It is to be noted that the compound (I) and the other compounds may include one or more stereoisomer(s) such as optical isomer(s) and geometrical isomer(s) due to asymmetric carbon atoms and double bond(s), and all of such isomers and mixture thereof are included within the scope of this invention.

[0217] The object compound (I) and pharmaceutically acceptable salts thereof possess activities as vasopressin antagonistic activity, vasodilating activity, hypotensive activity, activity for inhibiting saccharide release in liver, activity for inhibiting growth of mesangium cells, water diuretic activity, platelet agglutination inhibitory activity, oxytocin antagonistic activity, and are useful for the treatment and/or prevention of hypertension, heart failure, renal insufficiency, edema, ascites, vasopressin parasecretion syndrome, hepatocirrhosis, hyponatremia, hypokalemia, diabetic, circulation disorder, oxytocin relating diseases [e.g. premature delivery, dysmenorrhea, endometritis, etc.] in human beings and animals.

[0218] In order to illustrate the usefulness of the object compound (I), the pharmacological data of the compound (I) are shown in the following.

Test 1

[0219] Vasopressin 1 (V1) receptor binding

(i) Test Method :

[0220] The rat liver was dissected and homogenized in 10 volume of ice cold 250 mM sucrose buffer containing 25 mM Tris-HCl (pH 7.4), 5 mM $MgCl_2$ and 0.1 mM phenylmethylsulfonyl fluoride (PMSF). The homogenate was centrifuged at 1000 xg for 10 minutes. The supernatant fraction was separated and centrifuged at 45,000 xg for 30 minutes. The remaining pellet was resuspended in 10 volume of ice cold 100 mM Tris-HCl (pH 7.4) buffer (containing 5 mM $MgCl_2$, 0.1% bovine serum albumin and 0.1 mM PMSF), and centrifuged at 45,000 xg for 30 minutes again. The final pellet was resuspended in 100 mM Tris-HCl buffer. The resulting membrane preparation was used immediately for the binding assay.

[0221] Competition assays were conducted at equilibrium (60 minutes at 25°C) by using 0.5 nM ^{3}H-vasopressin ([phenylalanyl-3,4,5-^{3}H]-vasopression; 40-87 Ci/mmol; New England Nuclear) in 100 mM Tris-HCl (pH 7.4) buffer. Nonspecific binding was determined by using 1 μM [d(CH_2)$_5$, Tyr^2(Me), Arg^8]-vasopressin (Peptide institute, Japan). After incubation, reaction was terminated by adding 5 ml of ice-cold 100 mM Tris-HCl (pH 7.4) buffer, and then filtered rapidly through Whatman glass filter (GF/C). The filter was washed 2 times with the same buffer (5 ml). The glass filter was mixed with liquid scintilation cocktail, and radioactivity was counted in a liquid scintilation counter (TRI-CARB 4530, Packard). Competition activity of the test compound was represented by IC_{50} values.

(ii) Test Results :

[0222]

Test Compound (Example No.)	IC_{50}(M)
2-2)	3.9×10^{-9}
2-21)	4.4×10^{-9}

Test 2

[0223] Vasopressin 2 (V2) receptor binding

(i) Test Method :

[0224] The medullopapillary region of male rat kidey was dissected and homogenized in 10 volume of ice cold 250 mM sucrose buffer containing 25 mM Tris-HCl (pH 7.4), 5 mM $MgCl_2$ and 0.1 mM phenylmethylsulfonyl fluoride (PMSF). The homogenate was centrifuged at 500 xg for 5 minutes. The supernatant fraction was separated and centrifuged at 45,000 xg for 30 minutes. The remaining pellet was resuspended in 10 volume of ice cold 100 mM Tris-HCl (pH 7.4) buffer (containing 5 mM $MgCl_2$, 0.1% bovine serum albumin and 0.1 mM PMSF), and centrifuged at 45,000 xg for 30 minutes again. The final pellet was resuspended in 100 mM Tris-HCl buffer. The resulting membrane preparation was used immediately for the binding assay.

[0225] Competition assays were conducted at equilibrium (2 hours at 25°C) by using 0.5 nM ^{3}H-vasopression ([phenylalanyl-3,4,5-^{3}H]-vasopression; 40-87 Ci/mmol; New England Nuclear) in 100 mM Tris-HCl (pH 7.4) buffer. Nonspecific binding was determined by using 1 μM [d(CH_2)$_5$, D-Ile^2, Ile^4, Arg^8]-vasopressin (Peninsula Laboratories, USA). After incubation, reaction was terminated by adding 5 ml of ice-cold 100 mM Tris-HCl (pH 7.4) buffer, and then filtered rapidly through Whatman glass filter (GF/C). The filter was washed 2 times with the same buffer (5 ml). The glass filter was mixed with liquid scintilation cocktail, and radioactivity was counted in a liquid scintilation counter (TRI-CARB 4530, Packard). Competition activity of the test compound was represented by IC_{50} values.

(ii) Test Results :

[0226]

Test Compound (Example No.)	IC_{50}(M)
2-4)	3.0×10^{-9}
15	1.8×10^{-9}
16-3)	2.3×10^{-9}
16-9)	3.3×10^{-9}
16-14)	2.7×10^{-9}
16-56)	5.1×10^{-9}

[0227] For therapeutic purpose, the compound (I) of the present invention can be used in a form of pharmaceutical preparation containing one of said compounds, as an active ingredient, in admixture with a pharmaceutically acceptable carrier such as an organic or inorganic solid, semi-solid or liquid excipient suitable for oral, parenteral or external (topical)administration. The pharmaceutical preparations may be capsules, tablets, dragees, granules, suppositories, solution, lotion, suspension, emulsion, ointment, gel, or the like. If desired, there may be include in these preparations, auxiliary substances, stabilizing agents, wetting or emulsifying agents, buffers and other commonly used additives.

[0228] While the dosage of the compound (I) will vary depending upon the age and condition of the patient, an average single dose of about 0.1 mg, 1 mg, 10 mg, 50 mg, 100 mg, 250 mg, 500 mg and 1000 mg of the compound (I) may be effective for treating the above-mentioned diseases. In general, amounts between 0.1 mg/body and about 1,000 mg/body may be administered per day.

[0229] The following Preparations and Examples are given for the purpose of illustrating this invention.

[0230] In the following Preparations, Kieselgel Art. 5715 (Trademark : manufactured by E. Merck) (thickness : 0.25

mm) was used as TLC plate.

Preparation 1

[0231] To a solution of 1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (0.87 g) and triethylamine (0.55 g) in dichloromethane (5 ml) was added a solution of 4-nitrobenzoyl chloride (1.00 g) in dichloromethane (5 ml) at ambient temperature. After being stirred at ambient temperature for 2 hours, the solution was washed successively with 0.5N hydrochloric acid, saturated sodium bicarbonate aqueous solution, and brine. The organic layer was dried over magnesium sulfate, filtered and the solvents was evaporated. Trituration with a mixture of diethyl ether and diisopropyl ether (1:1) of a crude product afforded 5-(4-nitrobenzoyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (1.60 g) as a slightly brown powder.

mp : 225-230°C

Preparation 2

[0232] The following compounds were obtained according to a similar manner to that of Preparation 1.

1) 5-(4-Nitrobenzoyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 2.61-3.00 (2H, m), 3.90 (1H, br), 4.89 (1H, br), 6.71 (1H, d, J=8Hz), 6.90 (1H, t, J=8Hz), 7.01-7.77 (2H, m), 7.35 (2H, d, J=8.5Hz), 8.02 (2H, d, J=8.5Hz), 8.52 (1H, s)

2) 4-(4-Nitrobenzoyl)-1,2,3,4-tetrahydroquinoxalin-2-one
NMR (DMSO-d_6, δ) : 4.43 (2H, s), 6.73 (2H, br), 7.00-7.16 (2H, m), 7.64 (2H, d, J=8.5Hz), 8.20 (2H, d, J=8.5Hz)

3) 4-(3-Methoxy-4-nitrobenzoyl)-1,2,3,4-tetrahydroquinoxalin-2-one
NMR ($CDCl_3$, δ) : 3.85 (3H, s), 4.62 (2H, s), 6.65 (1H, br), 6.83 (1H, ddd, J=9, 9, 1Hz), 6.94 (1H, dd, J=9, 1Hz), 7.02 (1H, dd, J=8, 1Hz), 7.10-7.21 (2H, m), 7.72 (1H, d, J=8Hz), 9.35 (1H, s)

4) 7-Methyl-5-(4-nitrobenzoyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 2.05 (3H, s), 2.60-2.90 (2H, m), 3.80-3.93 (1H, br), 4.78-4.98 (1H, br), 6.52 (1H, s), 7.02 (2H, s), 7.37 (2H, d, J=10Hz), 8.03 (2H, d, J=10Hz), 8.07-8.17 (1H, br s)

5) 8-Chloro-5-(4-nitrobenzoyl)-1,3,4,5-tetrahydro-1.5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 2.70-2.86 (2H, m), 3.80-3.95 (1H, br), 4.75-4.96 (1H, br), 6.67 (1H, d, J=9Hz), 6.89 (1H, dd, J=1, 9Hz), 7.16 (1H, d, J=1Hz), 7.38 (2H, d, J=9Hz), 8.07 (3H, d, J=9Hz)

6) 8-Methyl-5-(4-nitrobenzoyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 2.30 (3H, s), 2.60-2.92 (2H, m), 3.78-3.95 (1H, m), 4.77-4.97 (1H, m), 6.59 (1H, d, J=8Hz), 6.69 (1H, d, J=8Hz), 6.94 (1H, s), 7.36 (2H, d, J=9Hz), 8.03 (2H, d, J=9Hz), 8.26-8.32 (1H, br s)

7) 8-Methoxy-5-(4-nitrobenzoyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 2.60-2.74 (1H, m), 2.75-2.92 (1H, m), 3.77 (3H, s), 3.85 (1H, dd, J=5, 12Hz), 4.78-4.96 (1H, m), 6.42 (1H, dd, J=3, 9Hz), 6.59-6.66 (2H, m), 7.36 (2H, d, J=9Hz), 8.02 (2H, d, J=9Hz), 8.04-8.11 (1H, br s)

8) 5-(2-chloro-4-nitrobenzoyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 2.60-3.04 (2H, m), 3.69-4.06 (1H, m), 4.87-5.22 (1H, m), 6.84-7.15 (3H, m), 7.15-7.47 (2H, m), 7.92 (1H, d, J=9Hz), 8.11 (1H, s), 8.49 (1H, s)

9) 5-(4-Nitrobenzoyl)-1,3,4,5-tetrahydro-1,5-benzodiazepine-2(2H)-thione
NMR ($CDCl_3$, δ) : 3.00-3.40 (2H, m), 3.85-4.10 (1H, m), 4.80-5.09 (1H, m), 6.76 (1H, br d, J=9Hz), 6.96-7.06 (1H, m), 7.19-7.46 (4H, m), 8.02 (2H, d, J=9Hz)

10) 4-Methyl-5-(4-nitrobenzoyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
Rf : 0.53 (10% methanol in chloroform)

11) 5-(4-Nitorbenzoyl)-8-trifluoromethyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.76-2.85 (2H, br), 3.85-3.96 (1H, br), 4.80-4.95 (1H, br), 6.87 (1H, d, J=8Hz), 7.18 (1H, d, J=8Hz), 7.40 (2H, d, J=10Hz), 7.41 (1H, s), 8.06 (2H, d, J=10Hz), 8.28-8.32 (1H, br s)

12) 7,8-Dimethyl-5-(4-nitrobenzoyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 1.96 (3H, s), 2.20 (3H, s), 2.57-2.93 (2H, m), 3.86 (1H, m), 4.87 (1H, m), 6.46 (1H, s), 6.92 (1H, s), 7.39 (2H, d, J=8.5Hz), 8.03 (2H, d, J=8.5Hz), 8.63 (1H, s)

13) 5-(3-Methyl-4-nitrobenzoyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 2.46 (3H, s), 2.60-3.00 (2H, m), 3.83 (1H, m), 4.84 (1H, m), 6.72 (1H, d, J=7.5Hz), 6.87-7.00 (2H, m), 7.17-7.31 (2H, m), 7.68 (1H, d, J=7.5Hz), 8.45 (1H, s)

Preparation 3

[0233] To a solution of 3-methoxy-4-nitrobenzoic acid (800 mg) and catalytic amount of N,N-dimethylformamide in dichloromethane (8 ml) was added oxalyl chloride (0.7 ml) at 0°C and the solution was stirred at ambient temperature for 30 minutes followed by the removal of solvents to give a crude acid chloride. To a solution of 1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (658 mg) and triethylamine (821 mg) in dichloromethane (4 ml) was added a solution of the above acid chloride in dichloromethane (4 ml) at ambient temperature and the mixture was stirred at ambient temperature for 1 hour. The resultant mixture was filtered and the solid was washed with water and diethyl ether to give 5-(3-methoxy-4-nitrobenzoyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (1.29 g) as a colorless prisms.
mp : 195-200°C

Preparation 4

[0234] To a solution of 4-(4-nitrobenzoyl)-1,2,3,4-tetrahydroquinoxalin-2-one (595 mg) in N,N-dimethylformamide (20 ml) was added sodium hydride (60% in oil, 80 mg). After being stirred at ambient temperature for 30 minutes, 3-bromopropylphthalimide (537 mg) was added to the solution and the mixture was stirred at ambient temperature for 4 hours. The mixture was diluted with ethyl acetate and the solution was washed successively with water, diluted hydrochloric acid, water and brine, dried over magnesium sulfate, and evaporated in vacuo to give an oil. The oil was purified by silica gel column (1% methanol in chloroform) to give 4-(4-nitrobenzoyl)-1-(3-phthaloylaminopropyl)-1,2,3,4-tetrahydroquinoxalin-2-one (452 mg) as a pale yellow solid.
NMR ($CDCl_3$, δ) : 2.16 (2H, tt, J=7.5, 7.5Hz), 3.79 (2H, t, J=7.5Hz), 4.18 (2H, t, J=7.5Hz), 4.58 (2H, s), 6.62 (1H, br), 6.81 (1H, t, J=7Hz), 7.08-7.24 (2H, m), 7.67 (2H, d, J=8.5Hz), 7.74 (2H, m), 7.86 (2H, m), 8.82 (2H, d, J=8.5Hz)

Preparation 5

[0235] The following compounds were obtained according to a similar manner to that of Preparation 4.

1) 1-Dimethylaminoethyl-5-(4-nitrobenzoyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
mp : 128-131°C
NMR ($CDCl_3$, δ) : 2.26 (6H, s), 2.58-2.83 (4H, m), 3.80-4.00 (2H, m), 4.08-4.24 (1H, m), 4.78 (1H, ddd, J=5, 13, 13Hz), 6.65 (1H, d, J=8Hz), 6.91 (1H, dd, J=1, 8Hz), 7.25-7.35 (1H, m), 7.43 (1H, dd, J=1, 8Hz), 7.63 (2H, d, J=9Hz), 8.02 (1H, d, J=9Hz)

2) 1-Dimethylaminoethyl-5-(3-methoxy-4-nitrobenzoyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one mp : 98-102°C

3) 1-(2-Ethoxycarbonylethyl)-5-(4-nitrobenzoyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 1.26 (3H, t, J=7Hz), 2.52-3.10 (4H, m), 3.70-3.97 (1H, m), 4.02-4.40 (4H, m), 4.60-4.95 (1H, m), 6.58-6.82 (1H, m), 6.85-7.10 (1H, m), 7.20-7.72 (4H, m), 7.95-8.20 (2H, m)

4) 1-(3-Ethoxycarbonylpropyl)-5-(4-nitrobenzoyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 1.27 (3H, t, J=7Hz), 1.96-2.31 (2H, m), 2.36-2.55 (2H, m), 2.56-2.85 (2H, m), 3.76-4.13 (3H, m), 4.62-4.92 (1H, m), 6.62-6.82 (1H, m), 6.85-7.09 (1H, m), 7.26-7.65 (4H, m), 8.06 (2H, br d, J=9Hz)

5) 1-(1-Ethoxycarbonylethyl)-5-(4-nitrobenzoyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 1.17 (5/7 x 3H, t, J=7Hz), 1.33 (2/7 x 3H, t, J=7Hz), 1.67-1.92 (3H, m), 2.50-2.88 (2H, m), 3.75-3.96 (1H, m), 4.00-4.42 (2H, m), 4.43-4.70 (1H, m), 4.70-4.96 (1H, m), 6.69 (1H, br d, J=9Hz), 6.80-7.11 (1H,

m), 7.20-7.66 (4H, m), 8.02 (2H, br d, J=9Hz)

6) 1-(t-Butoxycarbonylmethyl)-4-(4-nitrobenzoyl)-1,2,3,4-tetrahydroquinoxalin-2-one
NMR ($CDCl_3$, δ) : 1.52 (9H, s), 4.68 (4H, s), 6.62 (1H, br), 6.81 (1H, t, J=8Hz), 6.93 (1H, dd, J=1, 8Hz), 7.18 (1H, dt, J= 1, 8Hz), 7.62 (2H, d, J=8.5Hz), 8.17 (1H, d, J=8.5Hz)

7) 5-(4-Nitrobenzoyl)-1-(4-phthaloylaminobutyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 1.73-1.92 (4H, m), 2.57-2.71 (2H, m), 3.70-3.88 (4H, m), 4.09 (1H, m), 4.75 (1H, m), 6.63 (1H, d, J=8Hz), 6.90 (1H, t, J=8Hz), 7.23-7.40 (4H, m), 7.64-7.73 (2H, m), 7.78-7.86 (2H, m), 8.08 (2H, d, J=8.5Hz)

8) 1-(3-Dimethylaminopropyl)-4-(4-nitrobenzoyl)-1,2,3,4-tetrahydroquinoxalin-2-one
NMR ($CDCl_3$, δ) : 1.82-2.02 (2H, m), 2.26 (6H, s), 2.39 (2H, t, J=7Hz), 4.08 (2H, t, J=7Hz), 4.58 (2H, s), 6.60 (1H, br), 6.80 (1H, br t, J=8Hz), 7.22 (2H, dd, J=1, 8Hz), 7.53 (2H, d, J=8.5Hz), 8.17 (2H, d, J=8.5Hz)

9) 1-(2-Dimethylaminoethyl)-4-(4-nitrobenzoyl)-1,2,3,4-tetrahydroquinoxalin-2-one
NMR ($CDCl_3$, δ) : 2.30 (3H, s), 2.62 (2H, t, J=7Hz), 4.19 (1H, t, J=7Hz), 4.61 (2H, s), 6.58 (1H, br), 6.80 (1H, m), 7.19 (2H, d, J=4Hz), 7.57 (2H, d, J=8.5Hz), 8.15 (2H, d, J=8.5Hz)

10) 1-(3-Dimethylaminopropyl)-5-(4-nitrobenzoyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 1.88-2.10 (3H, m), 2.27 (6H, s), 2.43 (2H, d, J=7Hz), 2.57-2.86 (2H, m), 3.78-3.90 (2H, m), 3.98 (2H, t, J=7Hz), 4.78 (1H, m), 6.67 (1H, d, J=8Hz), 6.93 (1H, t, J=8Hz), 7.25-7.42 (4H, m), 8.03 (2H, d, J=8.5Hz)

11) 1-(4-Dimethylaminoethyl)-4-(3-methoxy-4-nitrobenzoyl)-1,2,3,4-tetrahydroquinoxalin-2-one
NMR ($CDCl_3$, δ) : 2.30 (6H, s), 2.61 (2H, t, J=7Hz), 3.90 (3H, s), 4.18 (2H, t, J=7Hz), 4.57 (2H, s), 6.67 (1H, br), 6.80-6.94 (2H, m), 7.20-7.28 (3H, m), 7.68 (1H, d, J=8Hz)

12) 4-(4-Nitrobenzoyl)-1-(3-piperidinopropyl)-1,2,3,4-tetrahydroquinoxalin-2-one
NMR ($CDCl_3$, δ) : 1.46 (2H, m), 1.53-1.69 (4H, m), 1.78-2.02 (2H, m), 2.31-2.48 (6H, m), 4.09 (2H, t, J=7Hz), 4.56 (2H, s), 6.60 (1H, br), 6.78 (1H, t, J=8Hz), 7.16-7.33 (2H, m), 7.52 (2H, d, J=8.5Hz), 8.17 (2H, d, J=8.5Hz)

13) 7,8-Dimethyl-1-ethoxycarbonylmethyl-5-(4-nitrobenzoyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
Rf : 0.71 (10% methanol in chloroform)

14) 1-Ethoxycarbonylmethyl-7-methyl-5-(4-nitrobenzoyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 1.31 (3H, t, J=8Hz), 2.07 (3H, s), 2.60-2.89 (2H, m), 3.87 (1H, dd, J=5, 14Hz), 4.27 (2H, dq, J=1, 7Hz), 4.46 (1H, d, J=17Hz), 4.69-4.89 (1H, m), 4.66 (1H, d, J=17Hz), 6.48-6.52 (1H, br s), 7.05-7.18 (2H, m), 7.51 (2H, d, J=9Hz), 8.05 (2H, d, J=9Hz)

15) 8-Chloro-1-ethoxycarbonylmethyl-5-(4-nitrobenzoyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 1.34 (3H, t, J=8Hz), 2.67-2.89 (2H, m), 3.82-3.93 (1H, m), 4.29 (2H, q, J=7Hz), 4.50 (1H, d, J=16Hz), 4.65 (1H, d, J=16Hz), 4.67-4.88 (1H, m), 6.60-6.69 (1H, br d, J=8Hz), 6.90-6.98 (1H, br d, J=8Hz), 7.20-7.30 (1H, m), 7.52 (2H, d, J=9Hz), 8.08 (2H, d, J=9Hz)

16) 8-Chloro-1-ethoxycarbonylmethyl-5-(3-methyl-4-nitrobenzoyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
Rf : 0.73 (10% methanol in chloroform)

17) 8-Chloro-1-ethoxycarbonylmethyl-5-(3-methoxy-4-nitrobenzoyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
Rf : 0.74 (10% methanol in chloroform)

18) 1-Ethoxycarbonylmethyl-5-(3-methoxy-4-nitrobenzoyl)-8-methyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
Rf : 0.79 (10% methanol in chloroform)

19) 1-Ethoxycarbonylmethyl-8-methyl-5-(4-nitrobenzoyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 1.32 (3H, t, J=7Hz), 2.31 (3H, s), 2.59-2.86 (2H, m), 3.86 (1H, dd, J=5, 13Hz), 4.22-4.36 (2H, m), 4.45 (1H, d, J=17Hz), 4.68 (1H, d, J=17Hz), 4.70-4.89 (1H, m), 6.58 (1H, d, J=8Hz), 6.72 (1H, d, J=8Hz),

7.03 (1H, s), 7.49 (2H, d, J=9Hz), 8.03 (2H, d, J=9Hz)

20) 1-Ethoxycarbonylmethyl-8-methyl-5-(3-methyl-4-nitrobenzoyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
Rf : 0.67 (10% methanol in chloroform)

21) 1-Ethoxycarbonylmethyl-8-methoxy-5-(4-nitrobenzoyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
Rf : 0.72 (10% methanol in chloroform)

22) 5-(2-Chloro-4-nitrobenzoyl)-1-ethoxycarbonylmethyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 1.36 (3H, t, J=7Hz), 2.59-2.92 (2H, m), 3.77-4.00 (1H, m), 4.12-4.38 (1H, m), 4.30 (2H, q, J=7Hz), 4.74 (1H, d, J=16Hz), 4.98 (1H, dt, J=5, 14Hz), 6.90-7.08 (2H, m), 7.14-7.61 (3H, m), 7.92 (1H, d, J=9Hz), 8.12 (1H, s)

23) 5-(3-Benzyloxy-4-nitrobenzoyl)-1-ethoxycarbonylmethyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 1.28 (3H, t, J=7Hz), 2.57-2.86 (2H, m), 3.78-3.93 (1H, m), 4.22 (2H, q, J=7Hz), 4.38 (1H, d, J=11Hz), 4.62 (1H, d, J=11Hz), 4.67-4.88 (1H, m), 5.01 (1H, d, J=9Hz), 5.10 (1H, d, J=9Hz), 6.66 (1H, br d, J=9Hz), 6.87 (1H, br d, J=9Hz), 6.92-7.04 (1H, m), 7.15-7.46 (8H, m), 7.60 (1H, br d, J=9Hz)

24) 4,4-Dimethyl-1-ethoxycarbonylmethyl-5-(4-nitrobenzoyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
Rf : 0.72 (10% methanol in chloroform)

25) 1-Ethoxycarbonylmethyl-4-methyl-5-(4-nitrobenzoyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
Rf : 0.64 (10% methanol in chloroform)

26) 1-Ethoxycarbonylmethyl-5-(4-nitrobenzoyl)-8-trifluoromethyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 1.34 (3H, t, J=8Hz), 2.70-2.79 (2H, m), 3.88-3.98 (1H, br), 4.29 (2H, dd, J=8, 15Hz), 4.62 (2H, s), 4.65-4.83 (1H, br), 7.19-7.27 (1H, br), 7.50-7.60 (3H, m), 8.00-8.12 (3H, m)

27) 5-(4-Nitrobenzoyl)-1-(3-pyridylmethyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 2.68-2.81 (2H, m), 3.65-3.84 (1H, m), 4.69-4.87 (1H, m), 4.79 (1H, d, J=14Hz), 5.64 (1H, d, J=14Hz), 6.58 (1H, d, J=7.5Hz), 6.69 (1H, d, J=7.5Hz), 6.93 (1H, t, J=7.5Hz), 7.22-7.37 (3H, m), 7.48 (1H, dd, J=7.5, 1.5Hz), 7.77-7.89 (3H, m), 8.50-8.61 (2H, m)

28) 7,8-Dimethyl-1-ethoxycarbonylmethyl-5-(4-nitrobenzoyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 1.31 (3H, t, J=7.5Hz), 1.96 (3H, s), 2.19 (3H, s), 2.58-2.90 (2H, m), 3.84 (1H, m), 4.27 (2H, m), 4.42 (1H, d, J=15.5Hz), 4.67 (1H, d, J=15.5Hz), 4.80 (1H, m), 6.43 (1H, s), 7.00 (1H, s), 7.51 (2H, d, J=8.5Hz), 8.05 (2H, d, J=8.5Hz)

29) 1-(6-Chlorohexyl)-5-(4-nitrobenzoyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 1.36-1.57 (4H, m), 1.70-1.87 (4H, m), 2.55-2.79 (2H, m), 3.53 (2H, t, J=7.5Hz), 3.78-4.00 (3H, m), 4.78 (1H, m), 6.67 (1H, d, J=7.5Hz), 6.91 (1H, m), 7.27-7.41 (4H, m), 8.04 (2H, d, J=8.5Hz)

30) 1-Ethoxycarbonylmethyl-5-(3-methyl-4-nitrobenzoyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 1.30 (3H, t, J=7.5Hz), 2.46 (3H, s), 2.60-2.89 (2H, m), 3.88 (1H, m), 4.25 (2H, m), 4.43 (1H, d, J=17Hz), 4.71 (1H, d, J=17Hz), 4.78 (1H, m), 6.70 (1H, d, J=7.5Hz), 6.97 (1H, m), 7.10-7.32 (3H, m), 7.41 (1H, s), 7.72 (1H, d, J=7.5Hz)

31) 1-Methoxycarbonylmethyl-5-(4-nitrobenzoyl)-1,3,4,5-tetrahydrd-1,5-benzodiazepin-2(2H)-one
NMR (DMSO-d_6, δ) : 2.45-2.80 (2H, m), 3.70 (3H, s), 3.78 (1H, m), 4.52 (1H, d, J=17.2Hz), 4.60 (1H, m), 4.78 (1H, d, J=17.2Hz), 6.90-7.06 (2H, m), 7.25-7.50 (2H, m), 7.47 (2H, d, J=8.7Hz), 8.04 (2H, d, J=8.7Hz)

Preparation 6

[0236] To a suspension of sodium hydride (60% oil suspension, 154 mg) in tetrahydrofuran (4 ml) was added a solution of 5-(4-nitrobenzoyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (800 mg) in tetrahydrofuran (6 ml) at 0°C and the mixture was stirred at 0°C for 5 minutes. To the mixture was added ethyl bromoacetate (472 mg) and then

the mixture was stirred at ambient temperature overnight. The reaction was quenched with saturated ammonium chloride aqueous solution and the resultant mixture was diluted with ethyl acetate. The organic layer was washed with saturated sodium bicarbonate aqueous solution and brine, and then it was dried over magnesium sulfate. Filtration and evaporation afforded 1-ethoxycarbonylmethyl-5-(4-nitrobenzoyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (691 mg) as a slightly yellow amorphous.

NMR ($CDCl_3$, δ) : 1.33 (3H, t, J=7Hz), 2.62-2.90 (2H, m), 3.90 (1H, ddd, J=1, 7, 13Hz), 4.29 (2H, ddd, J=1, 7, 15Hz), 4.50 (1H, d, J=16Hz), 4.70 (1H, d, J=16Hz), 4.65-4.90 (1H, m), 6.72 (1H, d, J=9Hz), 6.90-7.02 (1H, br), 7.23-7.37 (2H, m), 7.50 (2H, d, J=9Hz), 8.03 (2H, d, J=9Hz)

Preparation 7

[0237] The mixture of 1-ethoxycarbonylmethyl-5-(4-nitrobenzoyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (667 mg), iron powder (469 mg), methanol (10 ml) and acetic acid (1 ml) was refluxed for 1 hour. The reaction mixture was cooled to ambient temperature and it was filtered through a bed of celite followed by the removal of methanol. The residue was diluted with chloroform and to the mixture was added saturated sodium bicarbonate aqueous solution followed by stirring for 10 minutes. The resulting mixture was filtered through a bed of celite and the organic layer was washed with brine. Drying the filtrate, and the removal of chloroform obtained a crude product. The crude product was triturated with a mixture of diisopropyl ether and n-hexane (1:1) to give 5-(4-aminobenzoyl)-1-ethoxycarbonylmethyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (610 mg) as a slightly brown powder.

mp : 80-83°C

NMR ($CDCl_3$, δ) : 1.31 (3H, t, J=7Hz), 2.56-2.88 (2H, m), 3.78-3.90 (3H, br s), 4.15-4.35 (3H, m), 4.60-4.80 (1H, m), 4.83 (1H, d, J=16Hz), 6.39 (2H, d, J=9Hz), 6.80 (1H, d, J=9Hz), 6.95-7.05 (2H, m), 7.03 (1H, d, J=9Hz), 7.26 (2H, s)

Preparation 8

[0238] The following compounds were obtained according to a similar manner to that of Preparation 7.

1) 5-(4-Aminobenzoyl)-1-dimethylaminoethyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 2.39 (6H, s), 2.50-2.75 (4H, m), 3.77-3.90 (3H, br), 3.92-4.15 (2H, m), 4.56-4.78 (1H, m), 6.40 (1H, d, J=9Hz), 6.79 (1H, d, J=9Hz), 6.99 (1H, dt, J=1, 8Hz), 7.12-7.26 (1H, m), 7.15 (1H, d, J=9Hz), 7.29 (1H, dd, J=1, 8Hz), 7.42 (1H, dd, J=1, 8Hz)

2) 5-(4-Aminobenzoyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
mp : 216-221°C

3) 5-(4-Amino-3-methoxy)-1-dimethylaminoethyl-1,3,4,5-benzodiazepin-2(2H)-one
Slightly yellow oil

4) 5-(4-Amino-3-methoxybenzoyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
Slightly yellow oil

5) 5-(4-Aminobenzoyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 2.67 (2H, br), 3.90-4.80 (2H, br), 6.38 (2H, d, J=8.5Hz), 6.78 (1H, dd, J=1, 8Hz), 6.90-7.24 (5H, m)

6) 5-(4-Aminobenzoyl)-1-(2-ethoxycarbonylethyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 1.26 (3H, t, J=7Hz), 2.45-2.77 (2H, m), 2.78-3.00 (2H, m), 3.71-4.05 (2H, m), 4.05-4.37 (5H, m), 4.50-4.80 (1H, m), 6.43 (1H, d, J=9Hz), 6.82 (1H, br d, J=9Hz), 6.94-7.20 (3H, m), 7.20-7.46 (3H, m)

7) 5-(4-Aminobenzoyl)-1-(3-ethoxycarbonylpropyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 1.23 (3H, t, J=7Hz), 1.63-2.81 (6H, m), 3.68-4.25 (5H, m), 4.52-4.78 (1H, m), 6.41 (2H, d, J=9Hz), 6.80 (1H, d, J=9Hz), 6.90-7.15 (3H, m), 7.21-7.46 (2H, m)

8) 5-(4-Aminobenzoyl)-1-(1-ethoxycarbonylethyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 1.13 (5/7 x 3H, t, J=7Hz), 1.31 (2/7 x 3H, t, J=7Hz), 1.72 (3H, d, J=7Hz), 2.41-2.83 (2H, m), 3.70-4.85 (7H, m), 6.32-6.53 (2H, m), 6.70-6.91 (1H, m), 6.92-7.53 (5H, m)

9) 4-(4-Aminobenzoyl)-1-(t-butoxycarbonylmethyl)-1,2,3,4-tetrahydroquinoxalin-2-one

NMR ($CDCl_3$, δ) : 1.46 (9H, s), 3.97 (2H, s), 4.58 (2H, s), 4.62 (2H, s), 6.52 (2H, d, J=8.5Hz), 6.77-6.88 (3H, m), 7.09 (1H, m), 7.27 (2H, d, J=8.5Hz)

10) 5-(4-Aminobenzoyl)-1-(3-dimethylaminopropyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 1.87-2.03 (3H, m), 2.23 (6H, s), 2.35-2.46 (2H, m), 2.51-2.64 (2H, m), 3.35-3.89 (3H, m), 4.03 (1H, m), 4.65 (1H, m), 6.40 (2H, d, J=8.5Hz), 6.79 (1H, d, J=8Hz), 6.98 (1H, ddd, J=8, 8, 1Hz), 7.07 (2H, d, J=8.5Hz), 7.20-7.35 (2H, m)

11) 5-(4-Aminobenzoyl)-1-(4-phthaloylaminobutyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 1.70-1.89 (4H, m), 2.48-2.72 (2H, m), 3.68-3.89 (4H, m), 3.80 (2H, s), 4.08 (1H, m), 4.64 (1H, m), 6.40 (2H, d, J=8.5Hz), 6.79 (1H, d, J=8Hz), 6.98 (1H, ddd, J=8, 8, 1Hz), 7.07 (2H, d, J=8.5Hz), 7.19-7.35 (2H, m), 7.65-7.76 (2H, m), 7.79-7.86 (2H, m)

12) 4-(4-Aminobenzoyl)-1-(3-phthaloylaminopropyl)-1,2,3,4-tetrahydroquinoxalin-2-one

13) 4-(4-Aminobenzoyl)-1-(3-dimethylaminopropyl)-1,2,3,4-tetrahydroquinoxalin-2-one
NMR ($CDCl_3$, δ) : 1.82-1.98 (2H, m), 2.23 (6H, s), 2.38 (2H, t, J=7Hz), 3.96 (2H, s), 4.06 (2H, t, J=7Hz), 4.51 (2H, s), 6.52 (2H, d, J=8.5Hz), 6.78-6.84 (2H, m), 7.06-7.15 (2H, m), 7.72 (2H, d, J=8.5Hz)

14) 4-(4-Aminobenzoyl)-1-(2-dimethylaminoethyl)-1,2,3,4-tetrahydroquinoxalin-2-one
NMR ($CDCl_3$, δ) : 2.32 (6H, s), 2.61 (2H, t, J=7Hz), 3.94 (2H, s), 4.15 (2H, t, J=7Hz), 4.53 (2H, s), 6.52 (2H, d, J=8.5Hz), 6.74-6.87 (2H, m), 7.09-7.18 (2H, m), 7.25 (2H, d, J=8.5Hz)

15) 1-(2-Dimethylaminoethyl)-4-(4-amino-3-methoxybenzoyl)-1,2,3,4-tetrahydroquinoxalin-2-one
NMR ($CDCl_3$, δ) : 2.31 (6H, s), 2.60 (2H, t, J=7Hz), 3.74 (2H, s), 4.10 (2H, s), 4.14 (2H, t, J=7Hz), 4.54 (2H, s), 6.49 (1H, d, J=8Hz), 6.78-6.85 (3H, m), 6.97 (1H, d, J=1Hz), 7.08-7.19 (2H, m)

16) 4-(4-Aminobenzoyl)-1-(3-piperidinopropyl)-1,2,3,4-tetrahydroquinoxalin-2-one
NMR ($CDCl_3$, δ) : 1.39-1.50 (2H, m), 1.53-1.66 (4H, m), 1.85-2.00 (2H, m), 2.33-2.49 (6H, m), 3.96 (2H, s), 4.06 (2H, t, J=7Hz), 4.50 (2H, s), 6.52 (2H, d, J=8.5Hz), 6.75-6.86 (2H, m), 7.06-7.28 (4H, m)

17) 5-(4-Aminobenzoyl)-7,8-dimethyl-1-ethoxycarbonylmethyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
Rf : 0.60 (10% methanol in chloroform)

18) 5-(4-Aminobenzoyl)-1-ethoxycarbonylmethyl-7-methyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 1.29 (3H, t, J=8Hz), 2.13 (3H, s), 2.52-2.83 (2H, m), 3.73-3.88 (2H, br s), 4.10-4.36 (3H, m), 4.50-4.82 (2H, m), 4.80 (1H, d, J=15Hz), 6.30-6.45 (2H, m), 6.59 (1H, s), 7.00-7.16 (4H, m)

19) 5-(4-Aminobenzoyl)-8-chloro-1-ethoxycarbonylmethyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 1.32 (3H, t, J=8Hz), 2.62-2.79 (2H, m), 3.72-3.91 (3H, m), 4.15-4.35 (3H, m), 4.54-4.90 (2H, m), 6.43 (2H, d, J=10Hz), 6.73 (1H, d, J=9Hz), 6.98 (1H, dd, J=2, 9Hz), 7.05 (2H, d, J=10Hz), 7.27 (1H, d, J=2Hz)

20) 5-(4-Amino-3-methylbenzoyl)-8-chloro-1-ethoxycarbonylmethyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
Rf : 0.56 (10% methanol in chloroform)

21) 5-(4-Amino-3-methoxybenzoyl)-8-chloro-1-ethoxycarbonylmethyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
Rf : 0.58 (10% methanol in chloroform)

22) 5-(4-Amino-3-methoxybenzoyl)-1-ethoxycarbonylmethyl-8-methyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
Rf : 0.65 (10% methanol in chloroform)

23) 5-(4-Aminobenzoyl)-1-ethoxycarbonylmethyl-8-methyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 1.30 (3H, t, J=8Hz), 2.32 (3H, s), 2.52-2.85 (2H, m), 3.73-3.88 (2H, br), 4.12-4.43 (4H, m), 4.55-4.90 (2H, m), 6.33-6.45 (2H, m), 6.67 (1H, d, J=8Hz), 6.80 (1H, d, J=8Hz), 7.04-7.13 (3H, m)

24) 5-(4-Amino-3-methylbenzoyl)-1-ethoxycarbonylmethyl-8-methyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
Rf : 0.55 (10% methanol in chloroform)

25) 5-(4-Aminobenzoyl)-1-ethoxycarbonylmethyl-8-methoxy-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
Rf : 0.52 (10% methanol in chloroform)

26) 5-(4-Amino-2-chlorobenzoyl)-1-ethoxycarbonylmethyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 1.32 (3H, t, J=7Hz), 2.49-2.91 (2H, m), 3.70-4.07 (4H, m), 4.20-4.40 (2H, m), 4.74-4.99 (2H, m), 6.28 (1H, d, J=9Hz), 6.46 (1H, br s), 6.72-7.46 (5H, m)

27) 5-(4-Amino-3-methoxybenzoyl)-1-ethoxycarbonylmethyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 1.29 (3H, t, J=7Hz), 2.52-2.91 (2H, m), 3.66 (3H, s), 3.77-3.94 (1H, m), 4.00 (2H, br s), 4.13-4.38 (3H, m), 4.59-4.80 (1H, m), 4.82 (1H, d, J=16Hz), 6.37 (1H, d, J=9Hz), 6.63 (1H, d, J=9Hz), 6.78-6.87 (2H, m), 6.96-7.09 (1H, m), 7.22-7.32 (2H, m)

28) 1-(4-Aminobenzoyl)-3-methyl-1,2,3,5-tetrahydro-1,3-benzodiazepin-4(4H)-one
NMR ($CDCl_3$, δ) : 3.06 (3H, s), 3.96 (2H, br s), 4.09 (2H, s), 5.37 (2H, s), 6.44 (2H, d, J=9Hz), 6.71 (1H, d, J=9Hz), 6.91-7.26 (5H, m)

29) 5-(4-Aminobenzoyl)-1,3,4,5-tetrahydro-1,5-benzodiazepine-2(2H)-thione
NMR (DMSO-d_6, δ) : 2.91 (2H, m), 3.81-4.45 (2H, m), 5.53 (2H, s), 6.26 (2H, d, J=9Hz), 6.78 (3H, m), 7.05 (1H, dd, J=9, 9Hz), 7.20 (1H, d, J=9Hz), 7.28 (1H, dd, J=9, 9Hz)

30) 1-(4-Aminobenzoyl)-5-ethoxycarbonylmethoxyimino-2,3,4,5-tetrahydro-lH-1-benzazepine
NMR ($CDCl_3$, δ) : 1.26 (3H, t, J=7Hz), 1.60-2.13 (2H, m), 2.77-3.00 (2H, m), 3.68-3.96 (1H, br s), 4.21 (2H, q, J=7Hz), 4.11-4.33 (1H, m), 4.79 (2H, s), 6.37 (2H, d; J=8Hz), 6.71 (1H, d, J=8Hz), 7.05 (2H, d, J=8Hz), 7.10-7.28 (2H, m), 7.49 (1H, d, J=8Hz)

31) 5-(4-Aminobenzoyl)-8-methoxy-11-oxo-6,11-dihydrodibenz[b,e]azepine
NMR ($CDCl_3$, δ) : 3.70-3.93 (2H, br s), 3.91 (3H, s), 5.00-5.45 (2H, br s), 6.38 (2H, d, J=8Hz), 6.72-7.35 (7H, m), 8.20-8.42 (2H, m)

32) 1-(4-Aminobenzoyl)-5-methyl-2,3,4,5-tetrahydropyrido[3,2-b][1,4]diazepine
NMR ($CDCl_3$, δ) : 1.96-2.18 (2H, br s), 3.15 (3H, s), 2.97-3.52 (2H, m), 3.78 (3H, br s), 4.43-4.80 (1H, m), 6.30-6.48 (3H, m), 6.77 (1H, br d, J=9Hz), 7.12 (2H, d, J=9Hz), 7.96-8.03 (1H, m)

33) 5-(4-Aminobenzoyl)-4,4-dimethyl-1-ethoxycarbonylmethyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 1.31 (3H, t, J=8Hz), 1.57 (3H, s), 1.90 (3H, s), 2.27 (1H, d, J=13Hz), 2.53 (1H, d, J=13Hz), 3.70-3.79 (2H, br s), 4.19-4.35 (3H, m), 4.89 (1H, d, J=18Hz), 6.35 (2H, d, J=9Hz), 6.78 (2H, d, J=10Hz), 7.02-7.20 (4H, m)

34) 5-(4-Aminobenzoyl)-4-methyl-1-ethoxycarbonylmethyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
Rf : 0.58 (10% methanol in chloroform)

35) 5-(4-Aminobenzoyl)-1-(3,4-dimethoxybenzenesulfonyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine
Rf : 0.58 (10% methanol in chloroform)

36) 5-(4-Aminobenzoyl)-1-ethoxycarbonylmethyl-8-trifluoromethyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 1.32 (3H, t, J=8Hz), 2.65-2.75 (2H, br), 3.86-3.90 (2H, s), 4.22-4.34 (4H, m), 6.41 (2H, d, J=8Hz), 6.93 (1H, d, J=9Hz), 7.06 (2H, d, J=8Hz), 7.26 (1H, d, J=9Hz), 7.53 (1H, s)

37) 5-(4-Aminobenzoyl)-1-(3-pyridylmethyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 2.61-2.80 (2H, m), 3.74-3.90 (3H, m), 4.67 (1H, m), 4.79 (1H, d, J=15Hz), 5.60 (1H, d, J=15Hz), 6.19 (2H, d, J=8.5Hz), 6.44 (1H, d, J=8.5Hz), 6.69 (1H, dd, J=7.5, 1.5Hz), 6.97 (1H, dt, J=1.5, 7.5Hz), 7.14-7.31 (2H, m), 7.41 (1H, dd, J=7.5, 1.5Hz), 7.86 (1H, m), 8.43-8.53 (2H, m)

38) 5-(4-Aminobenzoyl)-7,8-dimethyl-1-ethoxycarbonylmethyl-1,3,4,5-tetrahydro-1,5-benzodiazepine-2(2H)-one
NMR ($CDCl_3$, δ) : 1.28 (3H, t, J=7.5Hz), 2.01 (3H, s), 2.20 (3H, s), 2.50-2.83 (2H, m), 3.26 (1H, m), 3.32 (2H, br), 4.57 (1H, m), 4.80 (1H, d, J=15.5Hz), 6.39 (2H, d, J=8.5Hz), 6.53 (1H, s), 6.99 (1H, s), 7.08 (2H, d, J=8.5Hz)

39) 5-(4-Aminobenzoyl)-1-ethoxycarbonylmethyl-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine
NMR ($CDCl_3$, δ) : 1.31 (3H, t, J=7.5Hz), 2.01 (2H, m), 3.20 (2H, m), 3.60-3.80 (3H, m), 4.06 (2H, m), 4.25 (2H, q, J=7.5Hz), 4.67 (1H, m), 6.38 (2H, d, J=8.5Hz), 6.53-6.62 (2H, m), 6.71 (1H, d, J=7.5Hz), 7.00 (1H, m), 7.15 (2H, d, J=8.5Hz)

40) 5-(4-Aminobenzoyl)-1-(6-phthalimidohexyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one This product was used for next step without purification.

41) 1-Ethoxycarbonylmethyl-5-(4-amino-3-methylbenzoyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 1.30 (3H, t, J=7.5Hz), 2.02 (3H, s), 2.53-2.87 (2H, m), 3.69-3.90 (3H, m), 4.12-4.33 (3H, m), 4.69 (1H, m), 4.88 (1H, d, J=17Hz), 6.43 (1H, d, J=7.5Hz), 6.80 (1H, d, J=7.5Hz), 6.99 (1H, m), 7.08 (1H, m), 7.16-7.27 (3H, m)

42) 1-(4-Aminobenzoyl)-7-chloro-5-ethoxycarbonylmethyl-2,3,4,5-tetrahydro-1H-1-benzazepine
NMR ($CDCl_3$, δ) : 1.26 (3H, t, J=7.5Hz), 1.31-2.14 (4H, m), 2.59-3.01 (2H, m), 3.12 (1H, m), 3.78 (2H, br), 4.03-4.27 (3H, m), 4.52 (1H, m), 6.38 (2H, d, J=8.5Hz), 6.68 (1H, d, J=7.5Hz), 6.95 (1H, m), 7.03-7.20 (3H, m)

43) 1-(4-Aminobenzoyl)-5-ethoxycarbonylmethyl-2,3-dihydro-1H-1-benzazepine
NMR ($CDCl_3$, δ) : 1.23 (3H, t, J=7.5Hz), 2.37 (1H, m), 2.58 (1H, m), 3.34-3.50 (2H, m), 3.68-3.82 (3H, m), 4.11 (2H, m), 4.77 (1H, m), 6.24 (1H, d, J=5Hz), 6.38 (2H, d, J=8.5Hz), 6.72 (1H, dd, J=1.5, 7.5Hz), 6.97 (1H, dt, J=1.5, 7.5Hz), 7.10 (2H, d, J=8.5Hz), 7.16 (1H, dt, J=1.5, 7.5Hz), 7.38 (1H, dd, J=1.5, 7.5Hz)

44) 5-(4-Aminobenzoyl)-2-(4-methyl-1-piperazinyl)-3,4-dihydro-5H-1,5-benzodiazepine
NMR ($CDCl_3$, δ) : 2.33 (3H, s), 2.68 (2H, m), 3.58-3.91 (5H, m), 4.62 (2H, m), 6.38 (2H, d, J=8.5Hz), 6.61-6.72 (2H, m), 7.01 (1H, d, J=7.5Hz), 7.05-7.17 (3H, m)

45) 1-(4-Aminobenzoyl)-2,3-dimethylindoline
NMR ($CDCl_3$, δ) : 1.10 (3H, d, J=6.5Hz), 1.27 (3H, d, J=6.5Hz), 3.55 (1H, dq, J=6.5, 6.5Hz), 3.94 (2H, br), 4.74 (1H, dq, J=6.5, 6.5Hz), 6.66 (2H, d, J=8.5Hz), 6.93-7.03 (3H, m), 7.14 (1H, m), 7.47 (2H, d, J=8.5Hz)

46) 5-(4-Aminobenzoyl)-1-methoxycarbonylmethyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR (DMSO-d_6, δ) : 2.35-2.70 (2H, m), 3.60 (3H, s), 3.60 (1H, m), 4.40 (1H, m), 4.47 (1H, d, J=16.6Hz), 4.75 (1H, d, J=16.6Hz), 5.50 (2H, s), 6.27 (2H, d, J=8.6Hz), 6.82 (1H, m), 6.88 (2H, d, J=8.6Hz), 7.04 (1H, m), 7.25-7.38 (2H, m)

Preparation 9

[0239] A mixture of N-ethoxycarbonylmethyl-N-(4-nitrobenzoyl)-2-nitroaniline (500 mg) and iron powder (374 mg) in a mixture of ethanol (10 ml) and acetic acid (1 ml) was heated at 80°C for 3 hours and the solution was cooled to ambient temperature. The mixture was filtered through celite and the filtrate was evaporated in vacuo. The residue was dissolved in chloroform (20 ml) and the solution was neutralized with aqueous sodium hydrogen carbonate. The solution was filtered through celite and the organic filtrate was washed with brine. The solution was dried over magnesium sulfate and the solvent was evaporated in vacuo to give a crude oil. The oil was purified by silica gel column (10 g, 2% methanol in chloroform) to give 4-(4-aminobenzoyl)-1,2,3,4-tetrahydroquinoxalin-2-one (58 mg) as a pale yellow powder.
NMR (DMSO-d_6, δ) : 4.31 (2H, s), 5.71 (2H, br), 6.43 (2H, d, J=8.5Hz), 6.69-6.83 (2H, m), 6.98-7.09 (4H, m)

Preparation 10

[0240] A mixture of N-(2-ethoxycarbonylethyl)-4-methyl-2-nitroaniline (11.25 g) and iron powder (12.45 g) in a mixture of methanol (70 ml) and acetic acid (7 ml) was refluxed for 1 hour and the solution was cooled to ambient temperature. The mixture was filtered through celite and the filtrate was evaporated in vacuo. The residue was dissolved with chloroform (50 ml) and the solution was basified with saturated sodium bicarbonate aqueous solution. The solution was filtered through celite and the organic layer was washed with brine. The solution was dried over magnesium sulfate

and the solvent was removed. A mixture of the residue (8.00 g) in a mixture of concentrated hydrochloric acid (16 ml) and water (12 ml) was refluxed for 1 hour and the solution was cooled to ambient temperature. The mixture was basified with concentrated ammonium hydroxide and then the resulting solution was extracted with chloroform. Drying over magnesium sulfate, filtering and the removal of solvents afforded a crude product. The crude product was triturated with diethyl ether - isopropyl ether (1:1) to give 8-methyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (1.26 g) as a brown powder.

NMR ($CDCl_3$, δ) : 2.26 (3H, s), 2.70 (2H, t, J=7Hz), 3.58-3.70 (1H, br), 3.66 (2H, t, J=7Hz), 6.63-6.69 (2H, m), 6.80 (1H, dd, J=1, 8Hz), 7.52-7.60 (1H, br)

Preparation 11

[0241] The following compounds were obtained according to a similar manner to that of Preparation 10.

1) 7-Methyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 2.27 (3H, s), 2.72 (2H, t, J=6Hz), 3.67 (2H, t, J=6Hz), 3.69-3.82 (1H, br), 6.56 (1H, s), 6.62 (1H, dd, J=1, 8Hz), 6.74 (1H, d, J=8Hz), 7.58-7.67 (1H, br)

2) 8-Chloro-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 2.71 (2H, t, J=6Hz), 3.67 (2H, t, J=6Hz), 3.70-3.95 (1H, br), 6.68 (1H, d, J=9Hz), 6.88 (1H, d, J=9Hz), 6.95 (1H, s), 7.82-7.94 (1H, br)

3) 8-Methoxy-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
Rf : 0.29 (ethyl acetate)

4) 8-Trifluoromethyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 2.79 (2H, t, J=5Hz), 3.69 (2H, dd, J=5, 10Hz), 4.21-4.29 (1H, br), 6.73 (1H, d, J=8Hz), 7.05 (1H, s), 7.18 (1H, d, J=8Hz), 7.58-7.64 (1H, br s)

Preparation 12

[0242] To a solution of 4,4-dimethyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (1.0 g) in N,N-dimethylaniline (20 ml) was added 4-nitrobenzoyl chloride (0.98 g) at ambient temperature. The mixture was stirred at 150°C for 9 hours. The resulting mixture was diluted with chloroform and the organic layer was washed successively with 1N hydrochloric acid and saturated aqueous sodium bicarbonate. Drying, filtering and the removal of solvents afforded a crude product. The crude product was chromatographed on silica gel (1% methanol in chloroform) to give 4,4-dimethyl-5-(4-nitrobenzoyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (195 mg) as a slightly yellow solid.

NMR ($CDCl_3$, δ) : 1.65 (3H, s), 2.02 (3H, s), 2.29 (1H, dd, J=1, 19Hz), 2.70 (1H, d, J=19Hz), 6.70-6.90 (2H, m), 7.03-7.20 (2H, m), 7.35 (2H, d, J=9Hz), 7.96 (2H, d, J=9Hz)

Preparation 13

[0243] To a solution of 1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (700 mg) in pyridine (10 ml) was added 3,4-dimethoxybenzenesulfonyl chloride (1.07 g) and the mixture was stirred at ambient temperature for 2 hours. The resulting mixture was diluted with ethyl acetate, and then the organic solution was washed successively with 0.5N hydrochloric acid, saturated aqueous sodium bicarbonate solution and brine. Drying, filtering and the removal of solvents afforded a crude product. The crude product was triturated with a mixture of diethyl ether and n-hexane (1:1) to give 5-(3,4-dimethoxybenzenesulfonyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (1.33 g) as a yellow powder.

NMR ($CDCl_3$, δ) : 2.51 (2H, t, J=8Hz), 3.77 (3H, s), 3.87 (3H, s), 4.32 (2H, t, J=8Hz), 6.80 (1H, d, J=8Hz), 6.88 (2H, dd, J=3, 10Hz), 7.20 (2H, dd, J=2, 10Hz), 7.25-7.39 (2H, m), 7.67 (1H, dd, J=1, 8Hz)

Preparation 14

[0244] To a mixture of 2,3-dimethylindoline (736 mg) and triethylamine (0.836 ml) in dichloromethane (20 ml) was added p-nitrobenzoyl chloride (928 mg) and the solution was stirred at ambient temperature for 4 hours. The solution was washed successively with 1N hydrochloric acid, saturated aqueous sodium hydrogen carbonate, water and brine, and dried over magnesium sulfate. The solvent was evaporated in vacuo and the residue was solidified with n-hexane to give 2,3-dimethyl-1-(4-nitrobenzoyl)-indoline (83.2 g).

NMR ($CDCl_3$, δ) : 1.18 (3H, d, J=6.5Hz), 1.31 (3H, d, J=6.5Hz), 3.59 (1H, dq, J=6.5, 6.5Hz), 4.77 (1H, dq, J=6.5,

6.5Hz), 7.15-7.45 (6H, m), 7.63 (1H, d, J=8.5Hz)

Preparation 15

[0245] The following compounds were obtained according to a similar manner to that of Preparation 14.

1) 3-Methyl-1-(4-nitrobenzoyl)-1,2,3,5-tetrahydro-1,3-benzodiazepin-4(4H)-one
NMR ($CDCl_3$, δ) : 3.15 (3H, s), 4.13 (2H, s), 5.43 (2H, s), 6.54 (1H, d, J=9Hz), 6.94 (1H, t, J=9Hz), 7.14 (1H, t, J=9Hz), 7.25 (1H, d, J=9Hz), 7.42 (2H, d, J=9Hz), 8.10 (2H, d, J=9Hz)

2) 1-(3,4-Dimethoxybenzenesulfonyl)-5-(4-nitrobenzoyl)-2,3,4,5-tetrahydro-lH-1,5-benzodiazepin
Rf : 0.67 (10% methanol in chloroform)

3) 1-Ethoxycarbonylmethyl-5-(4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine
NMR ($CDCl_3$, δ) : 1.36 (3H, t, J=7.5Hz), 1.98 (1H, m), 2.16 (1H, m), 3.04-3.23 (2H, m), 3.61 (1H, m), 3.98 (1H, d, J=17Hz), 4.19 (1H, d, J=17Hz), 4.28 (2H, g, J=7.5Hz), 4.70 (1H, m), 6.59 (2H, d, J=5Hz), 6.77(1H, d, J=7.5Hz), 7.08 (1H, m), 7.51 (2H, d, J=8.5Hz), 8.00 (2H, d, J=8.5Hz)

4) 7-Chloro-5-ethoxycarbonylmethyl-1-(4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-1-benzazepine
NMR ($CDCl_3$, δ) : 1.26 (3H, t, J=7.5Hz), 2.72 (2H, dd, J=6, 16Hz), 2.98 (2H, dd, J=6, 16Hz), 4.22 (2H, q, J=7.5Hz), 1.20-4.52 (7H, m), 6.75 (1H, d, J=7.5Hz), 6.95 (1H, m), 7.13 (1H, m), 7.52 (2H, d, J=8.5Hz), 8.02 (2H, d, J=8.5Hz)

5) 2-(4-Methyl-1-piperazinyl)-5-(4-nitrobenzoyl)-3,4-dihydro-5H-1,5-benzodiazepine
NMR ($CDCl_3$, δ) : 1.83 (1H, m), 2.33 (3H, s), 2.50 (4H, m), 2.73 (1H, m), 3.62-3.92 (5H, m), 4.77 (1H, m), 6.55 (1H, d, J=7.5Hz), 6.64 (1H, t, J=7.5Hz), 7.02 (1H, d, J=7.5Hz), 7.15 (1H, t, J=7.5Hz), 7.40 (2H, d, J=8.5Hz), 8.00 (2H, d, J=8.5Hz)

Preparation 16

[0246] To a solution of 2,3,4,5-tetrahydro-1H-1,5-benzodiazepine (300 mg) and triethylamine (615 mg) in dichloromethane (5 ml) was added dropwise a solution of 4-nitrobenzoyl chloride (789 mg) in dichloromethane (5 ml) at ambient temperature, and then the mixture was stirred at ambient temperature for 18 hours. The resulting solution was diluted with dichloromethane and the organic layer was washed successively with 0.5N hydrochloric acid solution, saturated aqueous sodium bicarbonate solution and brine. Drying, filtering and the removal of solvents afforded a crude product. The crude product was triturated with diethyl ether - n-hexane (1:1) to give 1,5-bis(4-nitrobenzoyl)-1,3,4,5-tetrahydro-lH-1,5-benzodiazepine (790 mg) as a yellow powder.
Rf : 0.68 (10% methanol in chloroform)

Preparation 17

[0247] To a solution of 8-methoxy-11-oxo-6,11-dihydrodibenz[b,e]azepine (150 mg) in N,N-dimethylaniline (1 ml) was added 4-nitrobenzoyl chloride (140 mg) at 110°C. The mixture was stirred for 1 hour at the same temperature and diluted with ethyl acetate. The solution was washed successively with diluted hydrochloric acid and brine. The organic phase was dried over magnesium sulfate, and evaporated in vacuo to give crude 8-methoxy-5-(4-nitrobenzoyl)-11-oxo-6,11-dihydrodibenz[b,e]azepine (240 mg).
NMR ($CDCl_3$, δ) : 3.93 (3H, s), 4.80-5.90 (2H, br s), 6.70 (1H, br d, J=8Hz), 6.91-7.08 (2H, m), 7.20-7.46 (4H, m), 8.03 (2H, d, J=8Hz), 8.23-8.35 (1H, m), 8.43 (1H, d, J=8Hz)

Preparation 18

[0248] The following compounds were obtained according to a' similar manner to that of Preparation 3.

1) 5-(3-Benzyloxy-4-nitrobenzoyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 2.54-2.66 (1H, m), 2.71-2.88 (1H, m), 3.76-3.91 (1H, m), 4.71-4.92 (1H, m), 4.94-5.17 (2H, m), 6.66 (1H, d, J=9Hz), 6.78 (1H, d, J=9Hz), 6.92 (1H, m), 6.99-7.11 (2H, m), 7.20-7.29 (1H, m), 7.33-7.45 (5H, m), 7.60 (1H, d, J=9Hz)

2) 5-(3-Methyl-4-nitrobenzoyl)-8-methyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 2.32 (3H, s), 2.49 (3H, s), 2.60-2.89 (2H, m), 3.78-3.92 (1H, m), 4.74-4.93 (1H, m), 6.60 (1H, d, J=8Hz), 6.72 (1H, d, J=8Hz), 6.94 (1H, s), 6.99 (1H, d, J=10Hz), 7.33 (1H, s), 7.69 (1H, d, J=10Hz), 8.22-8.27 (1H, br s)

3) 5-(3-Methoxy-4-nitrobenzoyl)-8-methyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 2.32 (3H, s), 2.58-2.90 (2H, m), 3.75-3.93 (1H, m), 3.81 (3H, s), 4.73-4.92 (1H, m), 6.63 (1H, d, J=9Hz), 6.70-6.80 (2H, m), 6.94 (1H, s), 7.03 (1H, d, J=1Hz), 7.58 (1H, d, J=8Hz), 8.31 (1H, s)

4) 8-Chloro-5-(3-methoxy-4-nitrobenzoyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
Rf : 0.44 (10% methanol in chloroform)

5) 8-Chloro-5-(3-methyl-4-nitrobenzoyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 2.50 (3H, s), 2.60-2.84 (2H, m), 3.78-3.93 (1H, m), 4.76-4.90 (1H, m), 6.69 (1H, d, J=9Hz), 6.92 (1H, d, J=9Hz), 7.00 (1H, d, J=9Hz), 7.16 (1H, s), 7.35 (1H, s), 7.73 (1H, d, J=9Hz), 8.45-8.52 (1H, br s)

Preparation 19

[0249] To a solution of 2-(2-methylphenyl)benzoic acid (2.12 g) in dichloromethane (20 ml) were added oxalyl chloride (1.7 ml) and two drops of N,N-dimethylformamide at 0°C and the solution was stirred at ambient temperature for 1 hour. Dichloromethane was evaporated in vacuo to give an acid chloride and the oil was added to a mixture of ethyl 4-amino-3-chlorobenzoate (1.99 g) and pyridine (1.58 g) in dichloromethane (15 ml). The mixture was stirred at ambient temperature for 1 day, washed successively with diluted hydrochloric acid, water and brine, and dried over magnesium sulfate. The solvent was evaporated in vacuo to give ethyl 3-chloro-4-[2-(2-methylphenyl)benzoylamino]-benzoate (4.0 g).

NMR ($CDCl_3$, δ) : 1.37 (3H, t, J=7Hz), 2.18 (3H, s), 4.34 (2H, q, J=7Hz), 7.17-7.37 (5H, m), 7.45-7.64 (2H, m), 7.82 (1H, br s), 7.85-7.95 (2H, m), 8.02 (1H, d, J=9Hz), 8.59 (1H, d, J=9Hz)

Preparation 20

[0250] The following compounds were obtained according to a similar manner to that of Preparation 19.

1) Ethyl 3-chloro-4-[2-(2,4-dimethylphenyl)-benzoylamino]benzoate
NMR ($CDCl_3$, δ) : 1.38 (3H, t, J=7Hz), 2.14 (3H, s), 2.33 (3H, s), 4.34 (2H, q, J=7Hz), 7.02-7.13 (2H, m), 7.15-7.36 (2H, m), 7.43-7.65 (2H, m), 7.82-7.96 (3H, m), 8.02 (1H, d, J=8Hz), 8.63 (1H, d, J=8Hz)

2) Ethyl 4-[2-(2-methylphenyl)benzoylamino]-3-nitrobenzoate
NMR ($CDCl_3$, δ) : 1.40 (3H, t, J=7Hz), 2.24 (3H, s), 4.38 (2H, q, J=7Hz), 7.11-7.30 (4H, m), 7.37 (1H, d, J=8Hz), 7.45-7.66 (2H, m), 7.86 (1H, d, J=8Hz), 8.21 (1H, d, J=8Hz), 8.73 (1H, s), 8.86 (1H, d, J=8Hz), 10.16 (1H, br s)

3) Ethyl 4-[2-(2,4-dimethylphenyl)benzoylamino]-2-nitrobenzoate
NMR ($CDCl_3$, δ) : 1.32 (3H, t, J=7Hz), 2.06 (3H, s), 2.45 (3H, s), 4.33 (2H, q, J=7Hz), 6.94-7.13 (1H, m), 7.16-7.40 (5H, m), 7.42-7.73 (4H, m), 8.16 (1H, d, J=9Hz)

Preparation 21

[0251] To a solution of 2-(4-methylphenyl)benzoic acid (2.12 g) in dichloromethane (20 ml) were added oxalyl chloride (2.02 g) and a few drops of N,N-dimethylformamide and the mixture was stirred at ambient temperature for 1 hour. The solvent was evaporated in vacuo to give an acid chloride and the acid chloride was added to a mixture of methyl 6-aminonicotinate (761 mg) and triethylamine (2.09 ml) in dichloromethane (30 ml). After being stirred at ambient temperature for 6 hours, the solution was washed with water and brine, and dried over magnesium sulfate. The solvent was evaporated in vacuo to give a syrup and the syrup was solidified with diethyl ether to give methyl 6-{N,N-di-[2-(4-methylphenyl)benzoyl]amino}nicotinate (2.22 g).

NMR ($CDCl_3$, δ) : 2.41 (6H, s), 3.87 (3H, s), 6.77 (2H, d, J=7.5Hz), 7.06 (2H, dt, J=1.5, 7.5Hz), 7.15-7.34 (9H, m), 7.43 (4H, d, J=8.5Hz), 8.22 (1H, m), 8.78 (1H, m)

Preparation 22

[0252] To a mixture of 2-nitroaniline (1.38 g) and triethylamine (1.67 ml) in dichloromethane (30 ml) were added 4-nitrobenzoyl chloride (1.85 g) and the solution was stirred at ambient temperature for 4 hours. The solution was washed successively with 1N hydrochloric acid, saturated aqueous sodium hydrogencarbonate, water and brine, and the organic layer was dried over magnesium sulfate. The solvent was evaporated in vacuo and the residue was solidified with n-hexane to give 2-nitro-N-(4-nitrobenzoyl)aniline (1.82 g).

NMR ($CDCl_3$, δ) : 7.64-7.83 (2H, m), 8.01 (2H, d, J=8.5Hz), 8.17-8.44 (4H, m)

Preparation 23

[0253] The following compound was obtained according to a similar manner to that of Preparation 22.

2-Chloro-3-(4-nitrobenzoyl)aminopyridine

NMR ($CDCl_3$, δ) : 7.36 (1H, m), 8.10 (2H, d, J=9Hz), 8.20 (1H, m), 8.40 (2H, d, J=9Hz), 8.43 (1H, br s), 8.88 (1H, d, J=9Hz)

Preparation 24

[0254] A mixture of 4-methyl-2-nitroaniline (10.0 g) and ethyl acrylate (9.87 g) in a mixture of concentrated hydrochloric acid (10 ml) and water (8.5 ml) was refluxed for 2 hours and the mixture was cooled to ambient temperature. The solution was basified with concentrated ammonium hydroxide and the resulting solution was extracted with chloroform. Drying over magnesium sulfate, filtering and the removal of solvents afforded N-(2-ethoxycarbonyl- ethyl)-4-methyl-5-nitroaniline (11.3 g) as a red oil.

Rf : 0.79 (10% methanol in chloroform)

Preparation 25

[0255] The following compounds were obtained according to a similar manner to that of Preparation 24.

1) 4-Chloro-N-(2-ethoxycarbonylethyl)-2-nitroaniline
Rf : 0.78 (10% methanol in chloroform)

2) N-(2-Ethoxycarbonylethyl)-4-methoxy-2-nitroaniline
Rf : 0.85 (10% methanol in chloroform)

3) N-(4-Ethoxycarbonylethyl)-2-nitro-4-trifluoromethylaniline
Rf : 0.75 (10% methanol in chloroform)

Preparation 26

[0256] A mixture of 5-methyl-2-nitroaniline (3.00 g), ethyl bromopropionate (5.35 g) and potassium carbonate (8.18 g) in N,N-dimethylformamide (20 ml) was stirred at 150°C for 4 hours and the suspension was cooled to ambient temperature. After being filtered, the filtrate was diluted with ethyl acetate and the solution was washed successively with saturated sodium bicarbonate aqueous solution and brine. Drying over magnesium sulfate, filtering and the removal of solvents afforded a crude product. The crude product was triturated with diethyl ether - n-hexane (1:1) to give N-(2-ethoxycarbonylethyl)-5-methyl-2-nitroaniline (2.83 g) as a yellow prisms.

NMR ($CDCl_3$, δ) : 1.30 (3H, t, J=8Hz), 2.37 (3H, s), 2.70 (2H, t, J=7Hz), 3.64 (2H, q, J=7Hz), 4.21 (2H, q, J=8Hz), 6.49 (1H, dd, J=1, 9Hz), 6.64 (1H, d, J=1Hz), 8.07 (1H, d, J=9Hz), 8.18-8.28 (1H, br)

Preparation 27

[0257] To a solution of 2-nitro-N-(4-nitrobenzoyl)aniline (910 mg) in N,N-dimethylformamide (20 ml) was added sodium hydride (60% in oil, 127 mg) and the solution was stirred at ambient temperature for 30 minutes. Ethyl bromoacetate (0.351 ml) was added to the solution and the mixture was stirred at ambient temperature overnight. The solution was diluted with ethyl acetate (30 ml) and the solution was washed successively with 1N hydrochloric acid, water and brine. The organic phase was dried over magnesium sulfate and the solvent was evaporated in vacuo to give an oil. The oil was solidified with diethyl ether to give [N-ethoxycarbonylmethyl-N-(4-nitrobenzoyl)]-2-nitroaniline (565 mg).

NMR ($CDCl_3$, δ) : 1.28 (3H, t, J=7Hz), 3.93 (1H, d, J=17.5Hz), 4.24 (2H, m), 5.15 (1H, d, J=17.5Hz), 7.38-7.52

(4H, m), 7.60 (1H, ddd, J=1, 8, 8Hz), 7.88 (1H, dd, J=1, 8Hz), 8.04 (2H, d, J=8.5Hz)

Preparation 28

[0258] To a solution of 2-chloro-3-(4-nitrobenzoyl)aminopyridine (1.93 g) in N,N-dimethylformamide (13 ml) was added sodium hydride (60 % in oil, 585 mg) and the solution was stirred at 0°C for ten minutes. 3-Dimethylaminopropyl chloride hydrochloride (1.16 g) was added to the solution and the mixture was stirred for 3 hours at 150°C. The solution was diluted with ethyl acetate and the solution was washed with successively with water, saturated aqueous sodium hydrogen carbonate and brine. The organic phase was dried over sodium sulfate and the solvent was evaporated in vacuo. The residue was purified by silica gel column chromatography (80 g, ethyl acetate:n-hexane = 1:3) to give 1-(4-nitrobenzoyl)-5-methyl-2,3,4,5-tetrahydropyrido[3,2-b][1,4]diazepine (450 mg).

NMR ($CDCl_3$, δ) : 2.01-2.28 (2H, br s), 3.17 (3H, s), 3.11-3.40 (2H, m), 3.73-3.96 (1H, m), 4.58-4.82 (1H, m), 6.35 (1H, dd, J=9, 9Hz), 6.71 (1H, d, J=9Hz), 7.38 (2H, d, J=9Hz), 7.34-7.56 (1H, m), 8.03 (2H, d, J=9Hz)

Preparation 29

[0259] A solution of 1-(4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-2-benzazepin-5-one (465 mg), hydroxylamine hydrochloride (209 mg) and pyridine (237 mg) in ethanol (10 ml) was stirred for 1.5 hours at 90°C. The solvent was evaporated and diluted with ethyl acetate and the solution was washed with successively water and brine. The organic phase was dried over magnesium sulfate and the solvent was evaporated in vacuo to give crude 5-hydroxyimino-1-(4-nitrobenzoyl)-2,3,4,5-tetrahydro-lH-1-benzazepine (500 mg).

NMR ($CDCl_3$, δ) : 1.60-2.23 (2H, m), 2.80-3.05 (2H, m), 3.31-3.56 (1H, m), 4.42-4.73 (1H, m), 6.69 (1H, d, J=8Hz), 7.04-7.20 (1H, m), 7.20-7.33 (1H, m), 7.38 (2H, d, J=8Hz), 7.51 (1H, d, J=8Hz), 7.98 (2H, d, J=8Hz), 9.09 (1H, br s)

Preparation 30

[0260] A solution of 5-hydroxyimino-1-(4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-1-benzazepine (500 mg) in N,N-dimethylformamide (10 ml) was treated with sodium hydride (72 mg, 60% w/w in mineral oil) at 0°C. The reaction mixture was stirred at 0°C for 5 minutes and then at ambient temperature for 30 minutes. Ethyl bromoacetate (301 mg) was added, and the reaction mixture was stirred for 2 hours. The reaction was quenched with aqueous hydrochloric acid and the mixture was diluted with ethyl acetate. The organic phase was washed with 0.5N hydrochloric acid, water, saturated aqueous sodium hydrogen carbonate, and brine. The organic solution was dried over magnesium sulfate and concentrated to give crude 5-ethoxycarbonylmethoxyimino-1-(4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-1-benzazepine. This product was taken on without further purification (700 mg).

NMR ($CDCl_3$, δ) : 1.31 (3H, t, J=7Hz), 1.62-2.18 (2H, m), 2.86-3.02 (2H, m), 3.28-3.61 (1H, m), 4.25 (2H, q, J=7Hz), 4.46-4.76 (1H, m), 4.80 (2H, s), 6.68 (1H, d, J=8Hz), 7.04-7.32 (2H, m), 7.39 (2H, d, J=8Hz), 7.40-7.56 (1H, m), 7.99 (2H, d, J=8Hz)

Preparation 31

[0261] To a solution of 1-ethoxycarbonylmethyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (173 mg) in tetrahydrofuran (5 ml) was added diborane dimethylsulfide complex (10 mol solution, 0.5 ml) and the mixture was stirred at ambient temperature for 8 hours. The solution was washed with water and brine, dried over magnesium sulfate. The solvent was evaporated in vacuo and a residue was purified by silica gel column to give 1-ethoxycarbonylmethyl-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine (125 mg) as a pale brown oil.

NMR ($CDCl_3$, δ) : 1.30 (3H, t, J=7.5Hz), 1.86 (2H, m), 3.16 (2H, t, J=5Hz), 3.27 (2H, t, J=5Hz), 3.97 (2H, s), 4.24 (2H, q, J=7.5Hz), 6.62-6.82 (4H, m)

Preparation 32

[0262] To a solution of naphthalene (15.5 g) in dimethoxyethane (100 ml) was added sodium metal (2.79 g) in portions at 0°C and the solution was stirred at the same temperature for 1 hour. The naphthilide was added to a solution of 7-chloro-5-ethoxycarbonylmethyl-1-(p-toluenesulfonyl)-2,3,4,5-tetrahydro-1H-1-benzazepine (9.89 g) in dimethoxyethane (400 ml) at -60°C and the solution was stirred at the same temperature for 30 minutes. The reaction mixture was quenched with water and the solution was extracted with chloroform. The extract was washed with brine and dried over magnesium sulfate. The solvent was evaporated in vacuo to give an oil and the crude oil was purified by silica gel column to give 7-chloro-5-ethoxycarbonylmethyl-2,3,4,5-tetrahydro-lH-1-benzazepine (2.31 g).

NMR ($CDCl_3$, δ) : 1.18 (3H, t, J=7.5Hz), 1.51-2.04 (4H, m), 2.67-2.90 (3H, m), 3.26 (1H, m), 3.44 (1H, m), 4.04

(2H, q, J=7.5Hz), 6.70 (1H, d, J=7.5Hz), 6.82 (1H, dt, J=1.5, 7.5Hz), 7.04 (1H, dt, J=1.5, 7.5Hz), 7.14 (1H, dd, J=1.5, 7.5Hz)

Preparation 33

[0263] To a solution of ethyl diethylphosphonoacetate (6.10 g) in tetrahydrofuran (50 ml) was added sodium hydride (60% in oil, 599 mg) and the solution was stirred at ambient temperature for 30 minutes. To the solution was added a solution of 1-(4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-1-benzazepine (3.10 g) in tetrahydrofuran (10 ml) dropwise and the mixture was stirred at ambient temperature for 5 hours. The solution was poured into water and the aqueous solution was extracted with ethyl acetate. The organic phase was washed with water and brine, and dried over magnesium sulfate. The solvent was evaporated in vacuo and the crude product was purified by silica gel column (100 g, 1% methanol in chloroform) to give 5-ethoxycarbonylmethylene-1-(4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-1-benzazepine (689 mg) and 5-ethoxycarbonylmethyl-1-(4-nitrobenzoyl)-2,3-dihydro-1H-1-benzazepine (905 mg).

5-Ethoxycarbonylmethylene-1-(4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-1-benzazepine

NMR ($CDCl_3$, δ) : 1.37 (3H, t, J=7.5Hz), 1.72-2.20 (2H, m), 2.39-2.80 (1H, m), 3.02 (1H, m), 3.36 (1H, m), 4.06-4.26 (2H, m), 4.50-4.98 (1H, m), 6.10 (1H, d, J=15Hz), 6.63 (1H, d, J=7.5Hz), 7.04 (1H, m), 7.18-7.37 (3H, m), 7.59 (1H, d, J=8Hz), 8.00 (2H, d, J=8.5Hz)

5-Ethoxycarbonylmethyl-1-(4-nitrobenzoyl)-2,3-dihydro-1H-1-benzazepine

MMR ($CDCl_3$, δ) : 1.27 (3H, t, J=7.5Hz), 2.41 (1H, m), 2.68 (1H, m), 3.94 (1H, d, J=17Hz), 3.55 (1H, m), 3.84 (1H, d, J=17Hz), 4.16 (2H, m), 4.80 (1H, m), 6.26 (1H, t, J=5Hz), 6.63 (1H, d, J=7.5Hz), 6.93 (1H, t, J=7.5Hz), 7.21 (1H, t, J=7.5Hz), 7.36 (1H, d, J=7.5Hz), 7.53 (2H, d, J=8.5Hz), 8.01 (2H, d, J=8.5Hz)

Preparation 34

[0264] To a mixture of 5-ethoxycarbonylmethylene-1-(4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-1-benzazepine (671 mg) and nickel chloride hexahydrate (419 mg) in a mixture of methanol (25 ml) and tetrahydrofuran (25 ml) was added sodium borohydride (601 mg) in portions at 0°C and the mixture was stirred at the same temperature for 30 minutes. The solution was filtered through a bed of celite and the filtrate was evaporated in vacuo. The residue was dissolved in chloroform and the solution was washed with water and brine, and dried over magnesium sulfate. The solvent was evaporated in vacuo to give a crude oil and the oil was subjected to silica gel column (30 g, 1% methanol in chloroform) to give 1-(4-aminobenzoyl)-5-ethoxycarbonylmethyl-2,3,4,5-tetrahydro-1H-1-benzazepine (500 mg).

FAB-MASS (m/z) : 353 (M+1)

Preparation 35

[0265] To a suspension of lithium aluminum hydride (168 mg) in tetrahydrofuran (10 ml) was added dropwise a solution of 5- (3, 4-dimethoxybenzenesulfonyl) -1,3,4, 5-tetrahydro-1,5-benzodiazepin-2(2H)-one (800 mg) at 0°C. The mixture was refluxed for 2.5 hours, and then the reaction was quenched with methanol. To the resulting mixture was added dropwise 2N sodium hydroxide solution (5 ml), and the mixture was stirred at ambient temperature for 30 minutes. The suspension was filtered through a bed of celite, and then the filtrate was diluted with ethyl acetate. The organic layer was washed with brine. Drying, filtering and the removal or solvents afforded a crude product. The crude product was chromatographed on silica gel (1% methanol in chloroform) to give 1-(3,4-dimethoxybenzenesulfonyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine (435 mg) as a yellow powder.

NMR ($CDCl_3$, δ) : 1.80 (2H, q, J=6Hz), 2.94 (2H, t, J=6Hz), 3.50-3.54 (1H, br), 3.74 (3H, s), 3.75-3.82 (2H, br), 3.92 (3H, s), 6.65 (1H, d, J=8Hz), 6.84 (1H, d, J=8Hz), 6.86 (1H, t, J=8Hz), 6.95 (1H, d, J=4Hz), 7.08 (1H, dd, J=6, 8Hz), 7.35 (1H, dd, J=4, 8Hz), 7.41 (1H, d, J=8Hz)

Preparation 36

[0266] A mixture of 1,5-bis(4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine (737 mg) and iron powder (738 mg) in a mixture of ethanol (10 ml) and acetic acid (1 ml) was refluxed for 2 hours and the solution was cooled to ambient temperature. The mixture was filtered through a bed of celite and the filtrate was evaporated in vacuo. The residue was dissolved in chloroform and the solution was basified with saturated aqueous sodium bicarbonate solution. The solution was filtered through a bed of celite, and then the filtrate was washed with brine. Drying, filtering and the removal of solvents afforded a crude product. The crude product was chromatographed on silica gel (eluent : 2% methanol in chloroform) to give 1,5-bis(4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine as a slightly yellow powder.

NMR ($CDCl_3$, δ) : 1.60-1.65 (4H, br s), 1.84-1.98 (2H, br), 3.80-3.88 (4H, br s), 6.49 (4H, d, J=8Hz), 7.02-7.10

(4H, br s), 7.26 (4H, d, J=8Hz)

Preparation 37

[0267] A solution of 5-(3-benzyloxy-4-nitrobenzoyl)-1-ethoxycarbonylmethyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (2.2 g), 10% palladium on carbon (220 mg) in ethanol (30 ml) and 1,4-dioxane (15 ml) was stirred under 4 atmospheric pressure of hydrogen at ambient temperature for 7 hours. The reaction mixture was filtered through a bed of celite, concentrated and purified by silica gel column chromatography (SiO_2 60 g, ethyl acetate:n-hexane = 2:1) to give 5-(4-amino-3-hydroxybenzoyl)-1-ethoxycarbonylmethyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (1.5 g).

NMR ($CDCl_3$, δ) : 1.28 (3H, t, J=7Hz), 2.54-2.67 (1H, m), 2.69-2.84 (1H, m), 3.78-4.03 (3H, m), 4.16-4.32 (3H, m), 4.41 (1H, d, J=10Hz), 4.60-4.77 (1H, m), 4.79 (1H, d, J=10Hz), 6.30 (1H, d, J=7Hz), 6.38 (1H, d, J=7Hz), 6.83 (1H, d, J=7Hz), 6.95-7.06 (1H, m), 7.16-7.33 (3H, m)

Preparation 38

[0268] The mixture of ethyl 3-chloro-4-[2-(2-methylphenyl)-benzoylamino]benzoate (4.0 g), 1N sodium hydroxide aqueous solution (15 ml) and ethanol (30 ml) was stirred for 5 hours at ambient temperature. Ethanol was removed in vacuo and the residue was washed with diethyl ether and the aqueous layer was acidified with 1N hydrochloric acid and diluted with ethyl acetate. The solution was washed with brine and dried over magnesium sulfate. Filtering and the removal of solvent afforded crude 3-chloro-4-[2-(2-methylphenyl)benzoylamino]benzoic acid (3.1 g).

NMR ($CDCl_3$ + CD_3OD, δ) : 2.19 (3H, s), 3.06 (2H, br s), 7.19-7.37 (5H, m), 7.45-7.66 (2H, m), 7.85-8.05 (3H, m), 8.57 (1H, d, J=9Hz)

Preparation 39

[0269] The following compounds were obtained according to a similar manner to that of Preparation 38.

1) 3-Chloro-4-[2-(2,4-dimethylphenyl)benzoylamino]-benzoic acid

NMR ($CDCl_3$, δ) : 2.16 (3H, s), 2.33 (3H, s), 6.99-7.14 (2H, m), 7.15-7.36 (2H, m), 7.43-7.66 (2H, m), 7.89-8.11 (4H, m), 8.67 (1H, d, J=8Hz)

2) 4-[2-(2-Methylphenyl)benzoylamino]-3-nitrobenzoic acid

NMR (DMSO-d_6, δ) : 2.10 (3H, s), 3.13-3.60 (2H, br s), 7.08-7.26 (4H, m), 7.28-7.40 (1H, m), 7.52-7.87 (4H, m), 8.18 (1H, d, J=8Hz), 8.37 (1H, s)

3) 4-[2-(2,4-Dimethylphenyl)benzoylamino]-2-nitrobenzoic acid

NMR ($CDCl_3$ + CD_3OD, δ) : 2.06 (3H, s), 2.42 (3H, s), 7.12-7.25 (3H, m), 7.26-7.38 (2H, m), 7.46 (1H, d, J=2Hz), 7.49-7.66 (2H, m), 7.75 (1H, d, J=9Hz), 8.06 (1H, dd, J=2, 9Hz)

Preparation 40

[0270] A solution of methyl 6-{N,N-di[2-(4-methylphenyl)-benzoyl]amino}nicotinate (2.10 g) in a mixture of 1N sodium hydroxide solution (40 ml) and methanol (40 ml) was heated at 70°C for 6 hours and methanol was removed under reduced pressure. The aqueous solution was adjusted to pH 5 with iN hydrochloric acid and the precipitated solid was filtered. The solid was washed with water and diethyl ether to give 6-(4-methylphenyl)benzoylaminonicotinic acid (831 mg).

NMR ($CDCl_3$ + CD_3OD, δ) : 2.43 (3H, s), 6.80 (1H, d, J=7.5Hz), 7.08 (1H, dt, J=1.5, 7.5Hz), 7.15-7.60 (7H, m), 8.20 (1H, m), 8.77 (1H, m)

Preparation 41

[0271] A mixture of 1-(6-chlorohexyl)-5-(4-nitrobenzoyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (675 mg) and potassium phthalimido (291 mg) in N,N-dimethylformamide (15 ml) was stirred at ambient temperature for 8 hours. The mixture was diluted with ethyl acetate and washed successively with 1N hydrochloric acid, aqueous sodium hydrogen carbonate and brine, and dried over magnesium sulfate. The solvent was evaporated in vacuo to give 5-(4-nitrobenzoyl)-1-(6-phthalimidohexyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (758 mg).

NMR ($CDCl_3$, δ) : 1.36-1.52 (4H, m), 1.63-1.89 (4H, m), 2.55-2.80 (2H, m), 3.67 (2H, t, J=7.5Hz), 3.77-3.97 (3H, m), 4.78 (1H, m), 6.69 (1H, d, J=7.5Hz), 6.91 (1H, m), 7.24-7.40 (4H, m), 7.65-7.75 (2H, m), 7.78-7.90 (2H, m), 8.04

(2H, d, J=8.5Hz)

Example 1

[0272] To a solution of 2-(4-methylphenyl)benzoic acid (140 mg) in dichloromethane (5 ml) were added oxalyl chloride (133 mg) and a few drop of N,N-dimethylformamide and the solution was stirred at ambient temperature for 2 hours. Dichloromethane was evaporated in vacuo to give an acid chloride as an oil and the oil was added to a mixture of 1-(4-aminobenzoyl)-1,2,3,4-tetrahydroquinoline (166 mg) and triethylamine (0.14 ml) in dichloromethane (20 ml). The mixture was stirred at ambient temperature for 2 hours, washed successively with diluted hydrogen chloride, water and brine and dried over magnesium sulfate. The solvent was evaporated in vacuo to give an oil and the oil was subjected to silica gel column (30 g, 1% methanol in chloroform) to give 1-{4-[2-(4-methylphenyl)benzoylamino]-benzoyl}-1,2,3,4-tetrahydroquinoline (202 mg) as an amorphous solid.

NMR ($CDCl_3$, δ) : 2.03 (2H, tt, J=7, 7Hz), 2.36 (3H, s), 2.82 (2H, t, J=7Hz), 3.88 (2H, t, J=7Hz), 6.67 (1H, d, J=8Hz), 6.87 (1H, dt, J=15, 8Hz), 6.95-7.60 (14H, m), 7.86 (1H, dd, J=1.5, 8Hz)

Example 2

[0273] The following compounds were obtained according to a similar manner to that of Example 1.

1) 5-Dimethylamino-1-{4-[2-(4-methylphenyl)benzoylamino]benzoyl}-2,3,4,5-tetrahydro-1H-benzazepine
NMR ($CDCl_3$, δ) : 1.30-3.05 (6H, m), 2.09 (3H, s), 2.32 (3H, s), 2.37 (3H, s), 4.07 (1H, m), 6.54 (1H, d, J=8Hz), 6.83-7.58 (15H, m), 7.83 (1H, d, J=8Hz)

2) 1-{4-[2-(4-Methylphenyl)benzoylamino]benzoyl}-2,3,4,5-tetrahydro-1H-benzazepine
NMR ($CDCl_3$, δ) : 1.49 (1H, m), 1.81-2.17 (3H, m), 2.33 (3H, s), 2.64-3.10 (3H, m), 5.00 (1H, m), 6.61 (1H, d, J=8Hz), 6.82-7.55 (15H, m), 7.84 (1H, d, J=8Hz)

3) 1-{4-[2-(4-Trifluoromethylphenyl)benzoylamino]-benzoyl}-1,2,3,4-tetrahydroquinoline
NMR ($CDCl_3$, δ) : 1.99 (2H, tt, J=7, 7Hz), 2.81 (2H, t, J=7Hz), 3.86 (2H, t, J=7Hz), 6.65 (1H, d, J=8Hz), 6.85 (1H, dt, J=1.5, 8Hz), 6.99 (1H, dt, J=1, 8Hz), 7.04-7.26 (6H, m), 7.39-7.65 (7H, m), 7.78 (1H, dt, J=1, 8Hz)

4) 1-{4-[2-(4-Methylphenyl)benzoylamino]benzoyl}-1,2,3,4-tetrahydroquinoxalin-3-one
NMR ($CDCl_3$, δ) : 2.36 (3H, s), 4.56 (2H, s), 6.68 (1H, d, J=8Hz), 6.79 (1H, ddd, J=1, 8, 8Hz), 7.93 (1H, dd, J=1, 8Hz), 7.00-7.13 (3H, m), 7.19-7.59 (9H, m), 7.88 (1H, dd, J=1, 8Hz), 8.57 (1H, br)

5) 1-(4-[2-(4-Chlorophenyl)benzoylamino]benzoyl}-1,2,3,4-tetrahydroquinoline
NMR ($CDCl_3$, δ) : 2.03 (2H, tt, J=7, 7Hz), 2.81 (2H, t, J=7Hz), 3.86 (2H, t, J=7Hz), 6.67 (1H, d, J=8Hz), 6.89 (1H, dd, J=8, 8Hz), 7.00 (1H, dd, J=8, 8Hz), 7.06-7.20 (4H, m), 7.21-7.32 (2H, m), 7.33-7.61 (6H, m), 7.77 (1H, dd, J=8, 2Hz)

6) 1-{4-[2-(4-Methoxyphenyl)benzoylamino]benzoyl}-1,2,3,4-tetrahydroquinoline
NMR ($CDCl_3$, δ) : 2.02 (2H, tt, J=7, 7Hz), 2.82 (2H, t, J=7Hz), 3.81 (3H, s), 3.88 (2H, t, J=7Hz), 6.69 (1H, d, J=8Hz), 6.81-7.20 (8H, m), 7.25 (2H, d, J=8Hz), 7.33-7.65 (5H, m), 7.85 (1H, dd, J=8, 2Hz)

7) 1-{4-[4-Methoxy-2-(4-methylphenyl)benzoylamino]-benzoyl}-1,2,3,4-tetrahydroquinoline
NMR ($CDCl_3$, δ) : 2.02 (2H, tt, J=7, 7Hz), 2.48 (3H, s), 2.81 (2H, t, J=7Hz), 3.87 (3H, s), 3.87 (2H, t, J=7Hz), 6.67 (1H, d, J=8Hz), 6.80-7.08 (7H, m), 7.09-7.38 (7H, m), 7.88 (1H, d, J=8Hz)

8) 1-{4-[2-(2,4-Dimethylphenyl)benzoylamino]benzoyl}-1,2,3,4-tetrahydroquinoline
NMR ($CDCl_3$, δ) : 2.03 (2H, tt, J=7, 7Hz), 2.06 (3H, s), 2.37 (3H, s), 2.83 (2H, t, J=7Hz), 3.86 (2H, t, J=7Hz), 6.66 (1H, d, J=8Hz), 6.78-7.06 (4H, m), 7.07-7.31 (8H, m), 7.42-7.63 (2H, m), 8.12 (1H, dd, J=8, 2Hz)

9) 1-{4-[2-(3,4-Dimethylphenyl)benzoylamino]benzoyl}-1,2,3,4-tetrahydroquinoline
NMR ($CDCl_3$, δ) : 2.04 (2H, tt, J=7, 7Hz), 2.23 (3H, s), 2.27 (3H, s), 2.83 (2H, t, J=7Hz), 2.88 (2H, t, J=7Hz), 6.65 (1H, d, J=8Hz), 6.86 (1H, dd, J=8, 8Hz), 6.92-7.06 (4H, m), 7.10-7.30 (5H, m), 7.34-7.60 (3H, m), 7.89 (1H, dd, J=8, 2Hz)

10) 1-{4-[2-(4-Hydroxyphenyl)benzoylamino]benzoyl}-1,2,3,4-tetrahydroquinoline

NMR ($CDCl_3$, δ) : 2.02 (2H, tt, J=7, 7Hz), 2.30 (1H, br s), 2.83 (2H, t, J=7Hz), 3.86 (2H, t, J=7Hz), 6.68 (1H, d, J=8Hz), 6.77-7.33 (12H, m), 7.35-7.58 (3H, m), 7.81 (1H, d, J=8Hz)

11) 1-{4-[2-(1-Naphthyl)benzoylamino]benzoyl}-1,2,3,4-tetrahydroquinoline
NMR ($CDCl_3$, δ) : 1.98 (2H, tt, J=7, 7Hz), 2.78 (2H, t, J=7Hz), 3.82 (2H, t, J=7Hz), 6.51-6.68 (3H, m), 6.81 (1H, dd, J=8, 8Hz), 6.89-7.20 (5H, m), 7.37-7.76 (8H, m), 7.85-8.00 (2H, m), 8.05-8.19 (1H, m)

12) 1-{4-[3-Methoxy-2-(4-methylphenyl)benzoylamino]-benzoyl}-1,2,3,4-tetrahydroquinoline
NMR ($CDCl_3$, δ) : 2.03 (2H, tt, J=7, 7Hz), 2.35 (3H, s), 2.82 (2H, t, J=7Hz), 3.78 (3H, s), 3.86 (2H, t, J=7Hz), 6.66 (1H, d, J=8Hz), 6.80-7.52 (14H, m)

13) 1-{4-[2-(2-Pyridyl)benzoylamino]benzoyl}-1,2,3,4-tetrahydroquinoline
NMR ($CDCl_3$, δ) : 2.04 (2H, tt, J=7, 7Hz), 2.83 (2H, t, J=7Hz), 3.89 (2H, t, J=7Hz), 6.72 (1H, d, J=7Hz), 6.87 (1H, dd, J=8, 8Hz), 7.00 (1H, dd, J=8, 8Hz), 7.16 (1H, d, J=8Hz), 7.21-7.65 (9H, m), 7.66-7.88 (2H, m), 8.55-8.66 (1H, m), 8.96 (1H, br s)

14) 1-{4-[2-(4-Ethylphenyl)benzoylamino]benzoyl}-1,2,3,4-tetrahydroquinoline
NMR ($CDCl_3$, δ) : 1.22 (3H, t, J=8Hz), 2.04 (2H, tt, J=7, 7Hz), 2.67 (2H, q, J=8Hz), 2.72 (2H, t, J=7Hz), 3.88 (2H, t, J=7Hz), 6.67 (1H, d, J=8Hz), 6.81-7.08 (5H, m), 7.09-7.63 (10H, m), 7.90 (1H, d, J=8Hz)

15) 1-{4-[2-(4-Propylphenyl)benzoylamino]benzoyl}-1,2,3,4-tetrahydroquinoline
NMR ($CDCl_3$, δ) : 0.93 (3H, t, J=8Hz), 1.63 (2H, tq, J=8, 8Hz), 2.04 (2H, tt, J=7, 7Hz), 2.61 (2H, t, J=8Hz), 2.84 (2H, t, J=7Hz), 3.88 (2H, t, J=7Hz), 6.67 (1H, d, J=8Hz), 6.81-7.06 (5H, m), 7.11-7.61 (10H, m), 7.92 (1H, d, J=8Hz)

16) 5-Dimethylamino-1-{4-[2-(2,4-dimethylphenyl)-benzoylamino]benzoyl}-2,3,4,5-tetrahydro-1H-benzazepine
NMR ($CDCl_3$, δ) : 1.10-2.50 (16H, m), 2.53-3.62 (2H, m), 3.90-5.25 (1H, m), 6.40-7.62 (15H, m), 8.00-8.15 (1H, m)

17) 5-Dimethylamino-1-{4-[2-(2-pyridyl)benzoylamino]-benzoyl}-2,3,4,5-tetrahydro-lH-benzazepine
NMR ($CDCl_3$, δ) : 1.11-2.54 (10H, m), 2.56-3.68 (2H, m), 3.94-5.25 (1H, m), 6.50-8.97 (17H, m)

18) 1-{4-[2-(2-Azidomethylphenyl)benzoylamino]benzoyl}-1,2,3,4-tetrahydroquinoline
NMR ($CDCl_3$, δ) : 2.02 (2H, tt, J=7, 7Hz), 2.82 (2H, t, J=7Hz), 3.86 (2H, t, J=7Hz), 4.34 (1H, d, J=12Hz), 4.60 (1H, d, J=12Hz), 6.66 (1H, d, J=8Hz), 6.79-7.47 (11H, m), 7.49-7.60 (2H, m), 7.74 (1H, br s), 7.88-7.98 (1H, m)

19) 1-{4-[2-Phenoxybenzoylamino]benzoyl}-1,2,3,4-tetrahydroquinoline
NMR ($CDCl_3$, δ) : 2.05 (2H, tt, J=7, 7Hz), 2.82 (2H, t, J=7Hz), 3.90 (2H, t, J=7Hz), 6.69 (1H, d, J=8Hz), 6.79-6.93 (2H, m), 6.98 (1H, dd, J=8, 8Hz), 7.06-7.62 (12H, m), 8.32 (1H, dd, J=8, 2Hz), 9.73 (1H, br s)

20) 1-{4-[2-(2-Methylphenyl)benzoylamino]benzoyl}-1,2,3,4-tetrahydroquinoline
NMR ($CDCl_3$, δ) : 2.04 (2H, tt, J=7, 7Hz), 2.10 (3H, s), 2.80 (2H, t, J=7Hz), 3.86 (2H, t, J=7Hz), 6.68 (1H, d, J=8Hz), 6.79-7.05 (4H, m), 7.08-7.45 (9H, m), 7.46-7.63 (2H, m), 8.11 (1H, dd, J=8, 2Hz)

21) 5-Dimethylamino-1-{4-[2-(2-methylphenyl)benzoylamino]benzoyl}-2,3,4,5-tetrahydro-1H-benzazepine
NMR ($CDCl_3$, δ) : 1.10-2.80 (13H, m), 2.95-3.65 (2H, m), 3.95-5.20 (1H, m), 6.48-6.77 (1H, m), 6.77-7.80 (15H, m), 8.07 (1H, br d, J=8Hz)

22) 1-Ethoxycarbonylmethyl-5-{4-[2-(4-methylphenyl)-benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
mp : 120-125°C
NMR ($CDCl_3$, δ) : 1.32 (3H, t, J=8Hz), 2.37 and 2.40 (total 3H, s), 2.25-2.90 (2H, m), 3.83 (1H, dd, J=6, 13Hz), 4.18-4.35 (3H, m), 4.60-4.90 (2H, m), 6.75 (1H, d, J=8Hz), 6.95 (4H, d, J=9Hz), 7.08-7.58 (11H, m), 7.82 (1H, dd, J=1, 9Hz)

23) 1-Ethoxycarbonylmethyl-5-{4-[2-(2-methylphenyl)-benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
mp : 127-130°C

NMR ($CDCl_3$, δ) : 1.33 (3H, t, J=7Hz), 2.08 (3H, s), 2.55-2.88 (2H, m), 3.85 (1H, dd, J=5, 11Hz), 4.17-4.35 (3H, m), 4.60-4.83 (1H, m), 4.70 (1H, d, J=17Hz), 6.73 (1H, d, J=9Hz), 6.85-7.04 (1H, m), 6.86 (2H, d, J=9Hz), 7.03-7.19 (3H, m), 7.20-7.43 (6H, m), 7.52 (1H, dt, J=6, 13Hz), 7.53 (1H, dt, J=6, 13Hz), 8.08 (1H, dd, J=1, 8Hz)

24) 1-(2-Dimethylaminoethyl)-5-{4-[2-(4-methylphenyl)-benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

mp : 178-181°C

NMR ($CDCl_3$, δ) : 2.29 (6H, s), 2.36 (3H, s), 2.50-2.75 (4H, m), 3.80 (1H, dd, J=5, 13Hz), 3.90-4.19 (2H, m), 4.68 (1H, dt, J=5, 13Hz), 6.70 (1H, d, J=7Hz), 6.90-7.12 (4H, br s), 7.18-7.60 (10H, m), 7.85 (1H, d, J=7Hz)

25) 1-(2-Dimethylaminoethyl)-5-{4-[2-(2-methylphenyl)-benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

mp : 210-213°C

NMR ($CDCl_3$, δ) : 2.10 and 2.11 (total 3H, s), 2.29 (6H, s), 2.50-2.75 (4H, m), 3.70-4.20 (3H, m), 4.65 (1H, dt, J=5, 12Hz), 6.60-6.72 (1H, br), . 6.80-7.00 (3H, m), 7.10-7.52 (12H, m), 8.08 (1H, dd, J=1, 7Hz)

26) 5-{4-[2-(2-Methylphenyl)benzoy]amino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

mp : 155-160°C

NMR ($CDCl_3$, δ) : 2.10 (3H, s), 2.60-2.80 (2H, m), 3.75-3.95 (1H, m), 4.65-4.83 (1H, m), 6.70 (1H, d, J=8Hz), 6.78-6.92 (3H, m), 7.00-7.15 (3H, m), 7.17-7.40 (6H, m), 7.53 (1H, dt, J=1, 8Hz), 7.56 (1H, dt, J=1, 7Hz), 8.02 (1H, dd, J=1, 7Hz)

27) 1-(2-Dimethylaminoethyl)-5-{3-methoxy-4-[2-(4-methylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

mp : 93-95°C

NMR ($CDCl_3$, δ) : 2.29 (6H, s), 2.39 (3H, s), 2.50-2.78 (4H, m), 3.50 (3H, s), 3.80 (1H, dd, J=5, 13Hz), 3.92-4.05 (2H, m), 4.69 (1H, dt, J=5, 12Hz), 6.60-6.80 (2H, m), 6.90-7.05 (2H, m), 7.15 (2H, d, J=9Hz), 7.23-7.58 (6H, m), 7.78 (2H, dd, J=7, 10Hz), 8.18 (1H, d, J=9Hz)

28) 1-(2-Dimethylaminoethyl)-5-{3-methoxy-4-[2-(2-methylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

mp : 173-175°C

NMR ($CDCl_3$, δ) : 2.10 and 2.18 (total 3H, s), 2.30 (6H, s), 2.50-2.78 (4H, m), 3.54 (3H, s), 3.80 (1H, dd, J=5, 12Hz), 3.90-4.03 (2H, m), 4.68 (1H, dt, J=5, 12Hz), 6.55-6.76 (2H, m), 6.87-7.00 (8H, m), 7.15-7.33 (5H, m), 7.40-7.58 (3H, m), 7.78-7.87 (1H, br), 7.95 (1H, dd, J=1, 8Hz), 8.15 (1H, d, J=9Hz)

29) 5-{3-Methoxy-4-[2-(4-methylphenyl)benzoylamino]-benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

mp : 126-129°C

NMR ($CDCl_3$, δ) : 2.35 (3H, s), 2.62-2.80 (2H, br), 3.40 (3H, s), 3.75-4.40 (1H, m), 4.65-4.90 (1H, m), 6.68 (1H, d, J=8Hz), 6.75 (2H, d, J=8Hz), 6.92 (1H, dd, J=1, 9Hz), 7.07-7.58 (7H, m), 7.68 (1H, s), 7.80 (1H, dd, J=1, 6Hz), 7.96 (1H, s), 8.20 (1H, d, J=9Hz)

30) 1-Ethoxycarbonylmethyl-5-{4-[2-(2,4-dimethylphenyl)-benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 1.39 (3H, t, J=7.5Hz), 2.00 and 2.03 (total 3H, s), 3.37 (3H, s), 2.52-2.85 (2H, m), 3.81 (1H, m), 4.18-4.34 (3H, m), 4.62-4.83 (2H, m), 6.71 (1H, m), 6.86 (2H, d, J=8.5Hz), 6.97 (1H, m), 7.08-7.28 (8H, m), 7.44-7.59 (2H, m), 8.07 (1H, dd, J=8, 1Hz)

31) 5-{4-[2-(4-Methylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.33 (3H, s), 2.69 (2H, br), 3.73-4.01 (1H, br), 4.53-4.94 (1H, br), 6.72 (1H, d, J=8Hz), 6.85-7.54 (14H, m), 7.80 (1H, dd, J=8, 1Hz), 8.22 (1H, s)

32) 1-(2-Ethoxycarbonylethyl)-5-{4-(2-(2-methylphenyl)-benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 1.27 (3H, t, J=7Hz), 2.00-2.17 (3H, m), 2.43-2.75 (2H, m), 2.76-2.97 (2H, m), 3.67-3.95 (1H, m), 4.05-4.38 (4H, m), 4.48-4.80 (1H, m), 6.60-7.70 (16H, m), 8.09 (1H, br d, J=9Hz)

33) 1-(3-Ethoxycarbonylpropyl)-5-{4-[2-(2-methylphenyl)-benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodi-

azepin-2(2H)-one

NMR ($CDCl_3$, δ) : 1.26 (3H, t, J=7Hz), 1.82-2.80 (9H, m), 3.80-4.23 (5H, m), 4.50-4.83 (1H, m), 6.60-7.75 (16H, m), 8.07 (1H, br d, J=9Hz)

34) 1-(1-Ethoxycarbonylethyl)-5-{4-[2-(2-methylphenyl)-benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 1.13 (5/7 x 3H, t, J=7Hz), 1.31 (2/7 x 3H, t, J=7Hz), 1.72 (3H, d, J=7Hz), 2.00-2.16 (3H, m), 2.43-2.80 (2H, m), 3.68-4.85 (5H, m), 6.55-7.68 (16H, m), 8.09 (1H, br d, J=9Hz)

35) 1-(t-Butoxycarbonylmethyl)-4-{4-[2-(4-methylphenyl)-benzoylamino]benzoyl}-1,2,3,4-tetrahydroquinoxalin-2-one

NMR ($CDCl_3$, δ) : 1.50 (9H, s), 2.38 (3H, s), 4.59 (2H, s), 4.64 (2H, s), 6.69-6.89 (3H, m), 7.02-7.57 (13H, m), 7.86 (1H, dd, J=8, 1Hz)

36) 1-(3-Dimethylaminopropyl)-5-{4-[2-(2-methylphenyl)-benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 1.87-1.99 (2H, m), 2.05 and 2.08 (total 3H, s), 2.23 (6H, s), 2.35-2.47 (2H, m), 2.53-2.73 (2H, m), 3.73-4.00 (3H, m), 4.66 (1H, m), 6.70 (1H, br), 6.82-6.99 (2H, m), 7.04-7.15 (2H, m), 7.21-7.38 (8H, m), 7.45-7.61 (2H, m), 8.08 (1H, d, J=8Hz)

37) 5-{4-[2-(2-Methylphenyl)benzoylamino]benzoyl}-1-(4-phthaloylaminobutyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 1.73-1.89 (4H, m), 2.06 and 2.08 (total 3H, s), 2.45-2.72 (2H, m), 3.67-4.01 (5H, m), 4.65 (1H, m), 6.69 (1H, br), 6.86 (2H, d, J=8.5Hz), 6.94 (1H, m), 7.02-7.13 (3H, m), 7.19-7.35 (7H, m), 7.45-7.59 (2H, m), 7.66-7.73 (2H, m), 7.78-7.85 (2H, m), 8.07 (1H, dd, J=8, 1Hz)

38) 4-{4-[2-(4-Methylphenyl)benzoylamino]benzoyl}-1-(3-phthaloylaminopropyl)-1,2,3,4-tetrahydroquinoxalin-2-one ,

NMR ($CDCl_3$, δ) : 2.16 (2H, tt, J=7.5, 7.5Hz), 2.33 (3H, s), 3.81 (2H, t, J=7.5Hz), 4.12 (2H, t, J=7.5Hz), 4.51 (2H, s), 6.71 (1H, d, J=8Hz), 6.80 (1H, dt, J=1, 8Hz), 7.01-7.55 (3H, m), 7.73 (2H, m), 7.80-7.88 (4H, m)

39) 1-(3-Dimethylaminopropyl)-4-{4-[2-(4-methylphenyl)-benzoylamino]benzoyl}-1,2,3,4-tetrahydroquinoxalin-2-one

NMR ($CDCl_3$, δ) : 1.86 (2H, tt, J=7.5, 7.5Hz), 2.22 (6H, s), 2.36 (3H, s), 2.39 (2H, t, J=7.5Hz), 4.05 (2H, t, J=7.5Hz), 4.54 (2H, s), 6.69-6.87 (2H, m), 7.01-7.57 (14H, m), 7.86 (1H, d, J=8Hz)

40) 1-(3-Dimethylaminopropyl)-4-{4-[2-(2-methylphenyl)-benzoylamino]benzoyl}-1,2,3,4-tetrahydroquinoxalin-2-one

NMR ($CDCl_3$, δ) : 1.80-1.95 (2H, m), 2.10 (3H, s), 2.24 (6H, s), 2.37 (2H, t, J=7Hz), 4.06 (2H, t, J=7Hz), 4.51 (2H, s), 6.67-6.84 (2H, m), 6.98 (2H, d. J=8.5Hz), 7.08-7.40 (10H, m), 7.48-7.61 (2H, m), 8.12 (1H, dd, J=2, 8Hz)

41) 1-(2-Dimethylaminoethyl)-4-{4-[2-(4-methylphenyl)-benzoylamino]benzoyl}-1,2,3,4-tetrahydroquinoxalin-2-one

NMR ($CDCl_3$, δ) : 2.30 (6H, s), 2.37 (3H, s), 2.59 (2H, t, J=7Hz), 4.15 (2H, t, J=7Hz), 4.52 (2H, s), 6.70 (1H, d, J=8Hz), 6.81 (1H, m), 7.02-7.58 (14H, m), 7.88 (1H, dd, J=1, 8Hz)

42) 1-(2-Dimethylaminoethyl)-4-{4-[2-(2-methylphenyl)-benzoylamino]benzoyl}-1,2,3,4-tetrahydroquinoxalin-2-one

NMR ($CDCl_3$, δ) : 2.11 (3H, s), 2.30 (6H, s), 2.60 (2H, t, J=7Hz), 4.15 (2H, t, J=7Hz), 4.52 (2H, s), 6.67-6.84 (2H, m), 6.98 (2H, d, J=8.5Hz), 7.12-7.40 (10H, m), 7.48-7.61 (2H, m), 8.12 (1H, dd, J=8, 2Hz)

43) 1-(2-Dimethylaminoethyl)-4-{3-methoxy-4-[2-(4-methylphenyl)benzoylamino]benzoyl)-1,2,3,4-tetrahydroquinoxalin-2-one

NMR ($CDCl_3$, δ) : 2.15 (3H, s), 2.32 (6H, s), 2.61 (2H, t, J=7Hz), 3.53 (3H, s), 4.15 (2H, t, J=7Hz), 4.53 (2H, m), 6.68-6.86 (3H, m), 6.93 (1H, d, J=1Hz), 7.13-7.17 (2H, m), 7.21-7.30 (4H, m), 7.43-7.57 (2H, m), 7.87 (1H, s), 7.99 (1H, dd, J=8, 1Hz), 8.31 (1H, d, J=8Hz)

44) 4-{4-[2-(2-Methylphenyl)benzoylamino]benzoyl}-1-(3-piperidinopropyl)-1,2,3,4-tetrahydroquinoxalin-2-one

NMR ($CDCl_3$, δ) : 1.40-1.50 (2H, m), 1.55-1.72 (4H, m), 1.84-2.00 (2H, m), 2.09 (3H, s), 2.35-2.46 (6H, m), 4.04 (2H, t, J=7Hz), 4.52 (2H, s), 6.68-6.82 (2H, m), 6.98 (2H, d, J=8.5Hz), 7.01-7.41 (9H, m), 7.48-7.61 (2H, m), 8.12 (1H, dd, J=1, 8Hz)

45) 1-{4-[2-(4-Fluoro-2-methylphenyl)benzoylamino]-benzoyl}-1,2,3,4-tetrahydroquinoline
NMR ($CDCl_3$, δ) : 1.96-2.11 (2H, m), 2.11 (3H, s), 2.84 (2H, t, J=7Hz), 3.88 (2H, t, J=7Hz), 6.67 (1H, d, J=8Hz), 6.86 (1H, dd, J=8, 8Hz), 6.94-7.42 (11H, m), 7.45-7.65 (2H, m), 7.98-8.10 (1H, m)

46) 1-{4-[2-(2-Ethylphenyl)benzoylamino]benzoyl}-1,2,3,4-tetrahydroquinoline
NMR ($CDCl_3$, δ) : 1.00 (3H, t, J=8Hz), 2.02 (2H, tt, J=7, 7Hz), 2.44 (2H, q, J=8Hz), 2.82 (2H, t, J=7Hz), 3.87 (2H, t, J=7Hz), 6.66 (1H, d, J=9Hz), 6.77-7.06 (5H, m), 7.07-7.64 (10H, m), 8.06-8.23 (1H, m)

47) 1-{4-[2-Fluoro-6-(2-methylphenyl)benzoylamino]-benzoyl}-1,2,3,4-tetrahydroquinoline
NMR ($CDCl_3$, δ) : 2.03 (2H, tt, J=7, 7Hz), 2.16 (3H, s), 2.81 (2H, t, J=7Hz), 3.86 (2H, t, J=7Hz), 6.68 (1H, d, J=8Hz), 6.88 (1H, dd, J=8, 8Hz), 7.00 (1H, dd, J=8, 8Hz), 7.05-7.63 (13H, m)

48) 1-{4-[2-(2,6-Dimethylphenyl)benzoylamino]benzoyl}-1,2,3,4-tetrahydroquinoline
NMR ($CDCl_3$, δ) : 2.03 (6H, s), 1.95-2.14 (2H, m), 2.82 (2H, t, J=7Hz), 3.85 (2H, t, J=7Hz), 6.68 (1H, d, J=8Hz), 6.80-7.05 (4H, m), 7.10-7.40 (7H, m), 7.42-7.68 (3H, m), 8.31 (1H, d, J=8Hz)

49) 1-{4-[2-(2-Cyanophenyl)benzoylamino]benzoyl}-1,2,3,4-tetrahydroquinoline
NMR ($CDCl_3$, δ) : 1.90-2.14 (2H, m), 2.84 (2H, t, J=7Hz), 3.87 (2H, t, J=7Hz), 6.71 (1H, d, J=8Hz), 6.88 (1H, dd, J=8, 8Hz), 7.00 (1H, dd, J=8, 8Hz), 7.14 (1H, d, J=8Hz), 7.20-7.85 (13H, m)

50) 7,8-Dimethyl-1-ethoxycarbonylmethyl-5-{4-[2-(4-methylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
Rf : 0.64 (10% methanol in chloroform)

51) 1-Ethoxycarbonylmethyl-7-methyl-5-{4-[2-(4-methylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 1.30 (3H,'t, J=8Hz), 2.10 (3H, s), 2.38 (3H, s), 2.53-2.85 (2H, m), 3.80 (1H, dd, J=5, 12Hz), 4.13-4.33 (3H, m), 4.59-4.78 (1H, m), 4.77 (1H, d, J=17Hz), 6.50-6.59 (1H, br), 6.90-7.33 (10H, m), 7.38-7.59 (3H, m), 7.83 (1H, dd, J=1, 8Hz)

52) 8-Chloro-1-ethoxycarbonylmethyl-5-{4-[2-(4-methylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 1.32 (3H, t, J=8Hz), 2.38 (3H, s), 2.60-2.80 (2H, m), 3.74-3.88 (1H, m), 4.15-4.36 (3H, m), 4.56-4.80 (1H, m), 4.76 (1H, d, J=17Hz), 6.68 (1H, d, J=8Hz), 6.92-7.04 (4H, m), 7.12 (2H, d, J=8Hz), 7.18-7.37 (4H, m), 7.38-7.58 (3H, m), 7.84 (1H, dd, J=1, 8Hz)

53) 8-Chloro-1-ethoxycarbonylmethyl-5-{3-methyl-4-[2-(4-methylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
Rf : 0.74 (10% methanol in chloroform)

54) 8-Chloro-1-ethoxycarbonylmethyl-5-{3-methoxy-4-[2-(4-methylphenyl)benzoylamino]benzoyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
Rf : 0.68 (10% methanol in chloroform)

55) 1-Ethoxycarbonylmethyl-5-{3-methoxy-4-[2-(4-methylphenyl)benzoylamino]benzoyl}-8-methyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 1.32 (3H, t, J=8Hz), 2.33 (3H, s), 2.36 (3H, s), 2.54-2.89 (2H, m), 3.49 (3H, s), 3.80 (1H, dd, J=5, 13Hz), 4.15-4.36 (3H, m), 4.60-4.82 (1H, m), 4.77 (1H, d, J=17Hz), 6.52-6.66 (2H, m), 6.78 (1H, d, J=8Hz), 6.94 (1H, s), 7.06 (1H, s), 7.11-7.34 (3H, m), 7.37-7.57 (3H, m), 7.73-7.85 (2H, m), 8.17 (1H, d, J=9Hz)

57) 1-Ethoxycarbonylmethyl-8-methyl-5-{4-[2-(4-methylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 1.30 (3H, t, J=8Hz), 2.32 (3H, s), 2.36 (3H, s), 2.55-2.84 (2H, m), 3.72-3.87 (1H, m), 4.15-4.34 (3H, m), 4.60-4.83 (1H, m), 4.79 (1H, d, J=17Hz), 6.56-6.65 (1H, m), 6.72-6.81 (1H, m), 6.90-7.58 (12H,

m), 7.84 (1H, dd, J=1, 8Hz)

58) 1-Ethoxycarbonylmethyl-8-methyl-5-{3-methyl-4-[2-(4-methylphenyl)benzoylamino)benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
Rf : 0.64 (10% methanol in chloroform)

59) 1-Ethoxycarbonylmethyl-8-methoxy-5-{4-[2-(4-methylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 1.31 (3H, t, J=8Hz), 2.38 (3H, s), 2.55-2.84 (2H, m), 3.63-3.80 (1H, m), 3.75 (3H, s), 4.10-4.32 (3H, m), 4.60-4.82 (1H, m), 4.80 (1H, d, J=17Hz), 6.45-6.70 (2H, m), 6.78 (1H, s), 6.92-7.57 (11H, m), 7.83 (1H, dd, J=1, 8Hz)

60) 5-{2-Chloro-4-[2-(2,4-dimethylphenyl)benzoylamino]-benzoyl}-1-ethoxycarbonylmethyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 1.34 (3H, t, J=7Hz), 2.02 and 2.06 (total 3H, s), 2.40 (3H, s), 2.52-2.89 (2H, m), 3.72-3.88 (1H, m), 4.00 (1H, d, J=16Hz), 4.30 (2H, q, J=7Hz), 4.84 (1H, d, J=16Hz), 4.77-5.01 (1H, m), 6.68-7.68 (14H, m), 8.01-8.11 (1H, m)

61) 1-Ethoxycarbonylmethyl-5-{3-methoxy-4-[2-(4-methylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 1.30 (3H, t, J=7Hz), 2.34 (3H, s), 2.52-2.92 (2H, m), 3.45 (3H, s), 3.74-3.95 (1H, m), 4.15-4.37 (3H, m), 4.57-4.89 (2H, m), 6.61 (1H, d, J=9Hz), 6.76 (1H, d, J=9Hz), 6.91 (1H, s), 6.94-7.07 (1H, m). 7.09-7.67 (9H, m), 7.74 (1H, br s), 7.81 (1H, d, J=9Hz), 8.19 (1H, d, J=9Hz)

62) 1-Ethoxycarbonylmethyl-5-{3-methoxy-4-[2-(2-methylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 1.31 (3H, t, J=7Hz), 2.08 and 2.13 (total 3H, s), 2.52-2.90 (2H, m), 3.48 (3H, s), 3.74-3.92 (1H, m), 4.10-4.37 (3H, m), 4.57-4.89 (2H, m), 6.43-7.59 (13H, m), 7.81 (1H, br s), 7.96 (1H, d, J=9Hz), 8.18 (1H, d, J=9Hz)

63) 1-Ethoxycarbonylmethyl-5-{3-methoxy-4-[2-(2,4-dimethylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1, 5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 1.30 (3H, t, J=7Hz), 2.04 and 2.10 (total 3H, s), 2.34 (3H, s), 2.50-2.92 (2H, m), 3.49 (3H, s), 3.74-3.94 (1H, m), 4.13-4.40 (3H, m), 4.57-4.91 (2H, m), 6.46-6.68 (1H, m), 6.68-7.34 (8H, m), 7.34-7.59 (3H, m), 7.88 (1H, s), 7.97 (1H, d, J=9Hz), 8.22 (1H, d, J=9Hz)

64) 5-{4-[2-(2,6-Dimethylphenyl)benzoylamino]benzoyl}-1-ethoxycarbonylmethyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
Rf : 0.57 (10% methanol in chloroform)

65) 3-Methyl-1-{4-[2-(2-methylphenyl)benzoylamino)-benzoyl)-1,2,3,5-tetrahydro-1,3-benzodiazepin-4(4H)-one
NMR ($CDCl_3$, δ) : 2.08 (3H, s), 3.06 (3H, s), 4.07 (2H, s), 5.35 (2H, s), 6.60 (1H, d, J=9Hz), 6.84-7.00 (3H, m), 7.04-7.44 (10H, m), 7.45-7.65 (2H, m), 8.11 (1H, d, J=9Hz)

66) 3-Methyl-1-{4-[2-(4-methylphenyl)benzoylamino]-benzoyl}-1,2,3,5-tetrahydro-1,3-benzodiazepin-4-(4H)-one
NMR ($CDCl_3$, δ) : 2.36 (3H, s), 3.08 (3H, s), 4.08 (2H, s), 5.36 (2H, s), 6.62 (1H, d, J=9Hz), 6.89-7.60 (15H, m), 7.85 (1H, d, J=9Hz)

67) 5-{4-[2-(4-Methylphenyl)benzoylamino]benzoyl}-2,3,4,5-tetrahydro-1,5-benzodiazepine-2(2H)-thione
NMR ($CDCl_3$, δ) : 2.35 (3H, s), 2.94-3.23 (2H, m), 3.70-3.83 (1H, m), 4.66-4.90 (1H, m), 6.68-6.80 (1H, m), 6.85-7.62 (15H, m), 7.79 (1H, d, J=9Hz)

68) 1-Ethoxycarbonylmethyl-5-{3-hydroxy-4-[2-(4-methylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahyro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 1.30 (3H, t, J=7Hz), 2.38 (3H, s), 2.54-2.66 (1H, m), 2.66-2.84 (1H, m), 2.86-2.97 (1H, m), 3.72-3.89 (1H, m), 4.18-4.36 (3H, m), 4.60-4.77 (1H, m), 4.81 (1H, d, J=10Hz), 6.26 (1H, d, J=8Hz), 6.56-7.06 (4H, m), 7.12-7.88 (11H, m)

69) 4,4-Dimethyl-1-ethoxycarbonylmethyl-5-{4-[2-(4-methylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
Rf : 0.78 (10% methanol in chloroform)

70) 1-Ethoxycarbonylmethyl-4-methyl-5-{4-[2-(4-methylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
Rf : 0.70 (10% methanol in chloroform)

71) 1-(3,4-Dimethoxybenzenesulfonyl)-5-{4-[2-(4-methylphenyl)benzoylamino]benzoyl}-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine
NMR ($CDCl_3$, δ) : 1.81-1.92 (2H, m), 1.86 (3H, s), 2.81-2.92 (2H, m), 3.76 (3H, s), 3.93 (3H, s), 4.02-4.18 (2H, m), 6.68-6.73 (1H, br), 6.87-7.03 (6H, m), 7.17-7.60 (12H, m), 7.83 (1H, d, J=8Hz)

72) 1-Ethoxycarbonylmethyl-5-{4-[2-(4-methylphenyl)-benzoylamino]benzoyl}-8-trifluoromethyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
Rf : 0.76 (10% methanol in chloroform)

73) 1-Ethoxycarbonylmethyl-5-{4-[2-(3-methylphenyl)-benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 1.30 (3H, t, J=7.5Hz), 2.30 (3H, s), 2.56-2.89 (2H, m), 3.82 (1H, m), 4.17-4.33 (3H, m), 4.62-4.84 (2H, m), 6.72 (1H, d, J=7.5Hz), 6.89-7.01 (4H, m), 7.08-7.57 (11H, m), 7.85 (1H, dd, J=7.5, 1.5Hz)

74) 5-{4-[2-(2-Methylphenyl)benzoylamino]benzoyl}-1-(3-pyridylmethyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 2.07 (3H, s), 2.58-2.83 (2H, m), 3.82 (1H, m), 4.69 (1H, m), 4.92 (1H, dd, J=9, 15Hz), 5.42 (1H, dd, J=5, 15Hz), 6.49-6.72 (4H, m), 6.92 (1H, t, J=7.5Hz), 7.10 (1H, s), 7.17-7.40 (9H, m), 7.48-7.61 (2H, m), 7.78 (1H, d, J=7.5Hz), 8.08 (1H, dd, J=1.5, 7.5Hz), 8.46 (1H, m), 8.57 (1H, m)

75) 7,8-Dimethyl-5-{4-[2-(2,6-dimethylphenyl)-benzoylamino]benzoyl}-1-ethoxycarbonylmethyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 1.29 (3H, t, J=7.5Hz), 1.96 (3H, s), 1.99 (3H, s), 2.02 (3H, s), 2.20 (3H, s), 2.47-2.82 (2H, m), 3.76 (1H, m), 4.12-4.33 (3H, m), 4.65 (1H, m), 4.78 (1H, d, J=15Hz), 6.46 (1H, br), 6.85 (2H, d, J=8.5Hz), 6.98 (1H, s), 7.08-7.36 (6H, m), 7.43 (1H, s), 7.48-7.62 (2H, m), 8.27 (1H, dd, J=1.5, 7.5Hz)

76) 1-Ethoxycarbonylmethyl-5-{4-[2-(4-methylphenyl)-benzoylamino]benzoyl}-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine
NMR ($CDCl_3$, δ) : 1.31 (3H, t, J=7.5Hz), 1.95 (1H, m), 2.09 (1H, m), 2.33 (3H, s), 3.08-3.23 (2H, m), 3.65 (1H, m), 3.98 (1H, d, J=17.5Hz), 4.12 (1H, d, J=17.5Hz), 4.26 (2H, q, J=7.5Hz), 4.68 (1H, m), 6.54 (2H, m), 6.71 (1H, d, J=7.5Hz), 6.86-6.93 (3H, m), 7.03 (1H, m), 7.14-7.55 (10H, m), 7.82 (1H, dd, J=1.5, 7.5Hz)

77) 1-(3-Dimethylaminopropyl)-5-{4-[2-(4-methylphenyl)-benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 1.86-2.05 (2H, m), 2.23 (6H, s), 2.37 (3H, s), 2.37-2.42 (2H, m), 2.50-2.76 (2H, m), 3.23-4.02 (3H, m), 4.57 (1H, m), 6.72 (1H, br), 6.90-7.02 (3H, m), 7.02-7.56 (13H, m), 7.84 (1H, dd, J=1.5, 7.5Hz)

78) 5-{4-[2-(2,6-Dimethylphenyl)benzoylamino]benzoyl}-1-ethoxycarbonylmethyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 1.27 (3H, t, J=7.5Hz), 2.05 (3H, s), 2.21 (3H, s), 2.47-2.85 (2H, m), 3.77 (1H, m), 4.15-4.37 (3H, m), 4.66 (1H, m), 4.76 (1H, d, J=15Hz), 6.46 (1H, br), 6.87 (2H, d, J=8.5Hz), 6.98 (1H, s), 7.11-7.35 (6H, m), 7.44 (1H, s), 7.50-7.63 (2H, m), 8.25 (1H, dd, J=1.5, 7.5Hz)

79) 5-{4-[2-(4-Methylphenyl)benzoylamino]benzoyl}-1-(6-phthalimidohexyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR ($CDCl_3$, δ) : 1.32-1.47 (4H, m), 1.57-1.78 (4H, m), 2.33 (3H, s), 2.50-2.72 (2H, m), 3.60-3.99 (4H, m), 4.63 (1H, m), 4.65 (1H, m), 6.74 (1H, d, J=7.5Hz), 6.95 (1H, m), 7.06-7.64 (11H, m), 7.72-7.89 (4H, m)

80) 1-(2-Acetoxyethyl)-5-{4-[2-(4-methylphenyl)-benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.03 (3H, s), 2.36 (3H, s), 2.50-2.78 (2H, m), 3.80 (1H, dd, J=6, 12.5Hz), 4.15 (2H, m), 4.41 (2H, m), 4.69 (1H, dt, J=6, 12.5Hz), 6.76 (1H, d, J=7.5Hz), 6.92-7.03 (4H, m), 7.10-7.57 (11H, m), 7.82 (1H, dd, J=1.5, 7.5Hz)

81) 1-Ethoxycarbonylmethyl-5-{4-[2-(2-trifluoromethylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 1.31 (3H, t, 7.5Hz), 2.52-2.88 (2H, m), 3.81 (1H, m), 4.15-4.82 (3H, m), 4.68 (1H, m), 4.78 (1H, d, J=17Hz), 6.70 (1H, d, J=7.5Hz), 6.90-7.36 (7H, m), 7.43-7.58 (4H, m), 7.77 (2H, m)

82) 1-Ethoxycarbonylmethyl-5-{4-[2-(2,4,6-trimethylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 1.31 (3H, t, J=7.5Hz), 1.93 (3H, s), 1.97 (3H, s), 2.37 (3H, s), 2.52-2.89 (2H, m), 3.82 (1H, m), 4.14-4.33 (3H, m), 4.70 (1H, m), 4.81 (1H, d, J=17Hz), 6.72 (1H, d, J=7.5Hz), 6.85 (1H, d, J=8.5Hz), 6.97 (1H, m), 7.01-7.17 (4H, m), 7.26 (2H, d, J=8.5Hz), 7.27 (1H, s), 7.44-7.60 (3H, m), 8.27 (1H, m)

83) 1-{4-[2-(2-Methylphenyl)benzoylamino]benzoyl}-2,3,4,5-tetrahydro-1H-1-benzazepin-5-one

NMR ($CDCl_3$, δ) : 2.06 (3H, s), 2.06-2.21 (3H, m), 2.77-2.96 (3H, m), 6.68 (1H, d, J=7.5Hz), 6.81 (2H, d, J=8.5Hz), 7.07 (2H, d, J=8.5Hz), 7.12-7.37 (7H, m), 7.43-7.62 (2H, m), 7.83 (1H, m), 8.10 (1H, m)

84) 1-Ethoxycarbonylmethyl-5-{3-methyl-4[2-(4-methylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 1.33 (3H, t, J=7.5Hz), 1.43 (3H, s), 2.35 (3H, s), 2.53-2.88 (2H, m), 3.82 (1H, m), 4.15-4.34 (3H, m), 4.70 (1H, m), 4.82 (1H, d, J=17Hz), 6.70-6.85 (3H, m), 6.97 (1H, m), 7.11-7.55 (9H, m), 7.83 (1H, dd, J=1.5, 7.5Hz), 8.02 (1H, d, J=7.5Hz)

85) 7-Chloro-5-ethoxycarbonylmethyl-1-{4-(2-(4-methylphenyl)benzoylamino]benzoyl}-2,3,4,5-tetrahydro-1H-1-benzazepine

NMR ($CDCl_3$, δ) : 1.27 (3H, t, J=7.5Hz), 2.33 (3H, s), 2.71 (1H, dd, J=6, 17.5Hz), 9.91 (1H, dd, J=6, 17.5Hz), 4.19 (1H, q, J=7.5Hz), 1.3-4.5 (7H, m), 6.53 (1H, d, J=7.5Hz), 6.86-6.95 (4H, m), 7.07-7.56 (10H, m), 7.84 (1H, d, J=7.5Hz)

86) 5-Ethoxycarbonylmethyl-1-{4-[2-{4-methylphenyl)-benzoylamino]benzoyl}-2,3,4,5-tetrahydro-1H-1-benzazepine

NMR ($CDCl_3$, δ) : 1.25 (3H, t, J=7.5Hz), 1.37 (1H, m), 1.78-2.09 (2H, m), 2.35 (3H, s), 2.64-3.00 (3H, m), 3.13 (1H, m), 3.51-3.79 (1H, m), 4.17 (2H, m), 4.51 (1H, m), 6.60 (1H, d, J=7.5Hz), 6.84-6.98 (4H, m), 7.10-7.55 (11H, m), 7.82 (1H, d, J=7.5Hz)

87) 5-Ethoxycarbonylmethyl-1-{4-[2-(2-methylphenyl)-benzoylamino]benzoyl)-2,3,4,5-tetrahydro-1H-1-benzazepine

NMR ($CDCl_3$, δ) : 1.27 (3H, t, J=7.5Hz), 2.08 (3x1/2H, s), 2.11 (3x1/2H, s), 2.67-3.01 (2H, m), 4.17 (2H, q, J=7.5Hz), 1.25-4.55 (7H, m), 6.59 (1H, d, J=7.5Hz), 6.81 (2H, d, J=8.5Hz), 6.91 (1H, m), 7.03-7.32 (10H, m), 7.44-7.59 (2H, m), 8.07 (1H, d, J=7.5Hz)

88) 5-Ethoxycarbonylmethyl-1-{4-[2-(4-methylphenyl)-benzoylamino]benzoyl}-2,3-dihydro-1H-1-benzazepine

NMR ($CDCl_3$, δ) : 1.23 (3H, t, J=7.5Hz), 2.32 (3H, s), 2.37 (1H, m), 2.60 (1H, m), 3.40 (1H, d, J=17.5Hz), 3.46 (1H, m), 3.75 (1H, d, J=17.5Hz), 4.14 (2H, m), 4.75 (1H, m), 6.22 (1H, t, J=5Hz), 6.64 (1H, d, J=7.5Hz), 6.84-6.97 (3H, m), 7.10-7.57 (12H, m), 7.81 (1H, dd, J=1.5, 7.5Hz)

89) 2-Dimethylamino-5-{4-[2-(4-methylphenyl)benzoylamino]benzoyl}-3,4-dihydro-5H-1,5-benzodiazepine

NMR ($CDCl_3$, δ) : 2.36 (3H, s), 2.57-2.69 (2H, m), 3.16 (6H, s), 3.85 (1H, dd, J=6, 16Hz), 4.67 (1H, dt, J=6, 16Hz), 6.55 (1H, d, J=7.5Hz), 6.64 (1H, t, J=7.5Hz), 6.86-6.93 (3H, m), 6.53 (1H, d, J=7.5Hz), 7.60-7.68 (5H, m), 7.29 (2H, d, J=8.5Hz), 7.39 (1H, t, J=7.5Hz), 7.05 (1H, d, J=7.5Hz), 7.52 (1H, t, J=7.5Hz), 7.84 (1H, d, J=7.5Hz)

90) 1-{4-[1-(4-Methylphenyl)-2-naphthoylamino]benzoyl}-1,2,3,4-tetrahydroquinoline

NMR ($CDCl_3$, δ) : 2.03 (2H, tt, J=7, 7Hz), 2.44 (3H, s), 2.83 (2H, t, J=7Hz), 3.86 (2H, t, J=7Hz), 6.66 (1H, d, J=8Hz), 6.86 (1H, dd, J=8, 8Hz), 6.93-7.07 (3H, m), 7.10-7.28 (4H, m), 7.35 (4H, s), 7.44 (1H, dd, J=8, 8Hz), 7.56 (1H, dd, J=8, 8Hz), 7.66 (1H, d, J=8Hz), 7.84-8.02 (3H, m)

91) 2,3-Dimethyl-1-{4-[2-(4-methylphenyl)benzoyl]-aminobenzoyl}indoline
NMR ($CDCl_3$, δ) : 1.05 (3H, d, J=6.5Hz), 1.09 (3H, d, J=6.5Hz), 2.38 (3H, s), 3.58 (1H, dq, J=6.5, 6.5Hz), 4.72 (1H, dq, J=6.5, 6.5Hz), 6.97-7.59 (16H, m), 7.99 (1H, dd, J=1.5, 7.5Hz)

92) 5-Dimethylamino-1-{6-[2-(4-methylphenyl)benzoyl]-aminonicotinoyl}-2,3,4,5-tetrahydro-1H-benzazepine
NMR ($CDCl_3$, δ) : 1.30-3.00 (6H, m), 2.08 (3H, s), 2.30 (3H, s), 2.37 (3H, s), 4.06 (1H, m), 6.56 (1H, d, J=8Hz), 6.95-8.20 (16H, m)

93) 1-Methoxycarbonylmethyl-5-{4-[2-(4-methylphenyl)-benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one
NMR (DMSO-d_6, δ) : 2.28 (3H, s), 2.40-2.75 (2H, m), 3.68 (3H, s), 3.72 (1H, m), 4.48 (1H, m), 4.51 (1H, d, J=17.1Hz), 4.76 (1H, d, J=17.1Hz), 6.80-7.40 (16H, m), 10.3 (1H, s)

Example 3

[0274] To a solution of 2-(1-pyrrolyl)benzoic acid (206 mg), diphenyl chlorophosphate (325 mg), 1-(4-aminobenzoyl)-1,2,3,4-tetrahydroquinoline (277 mg) in tetrahydrofuran (10 ml) was added triethylamine (333 mg) at 0°C. The resulting mixture was allowed to warm to ambient temperature where it was maintained for 5 hours. The solvent was evaporated and diluted with ethyl acetate and washed with water, saturated sodium bicarbonate aqueous solution and brine. The organic layer was dried over sodium sulfate and concentrated to give 1-{4-[2-(1-pyrrolyl)benzoylamino]benzoyl}-1,2,3,4-tetrahydroquinoline (280 mg).
NMR (DMSO-d_6, δ) : 1.94 (2H, tt, J=7, 7Hz), 2.81 (2H, t, J=7Hz), 3.74 (2H, t, J=7Hz), 6.17 (2H, dd, J=2, 2Hz), 6.77 (1H, d, J=8Hz), 6.86-7.10 (4H, m), 7.21 (1H, d, J=8Hz), 7.28 (2H, d, J=8Hz), 7.40-7.70 (6H, m)

Example 4

[0275] To a solution of 1-(carboxymethyl)-4-{4-[2-(4-methylphenyl)benzoylamino]benzoyl}-1,2,3,4-tetrahydroquinoxalin-2-one (100 mg) in dichloromethane (10 ml) were added triethylamine (0.030 ml) and diphenylphosphinic chloride (54.7 mg) and the solution was stirred at ambient temperature for 30 minutes. Triethylamine (0.030 ml) and 1-methylpiperazine (0.032 ml) were added to the solution and the mixture was stirred at ambient temperature for 3 hours. The solution was washed with water and brine and dried over magnesium sulfate. The organic solution was evaporated in vacuo and the residue was subjected to a silica gel column (10 g, 2% methanol in chloroform). The object fractions were evaporated in vacuo and the residue was solidified with diethyl ether to give 1-[(4-methyl-1-piperazinyl)carbonylmethyl]-4-{4-[2-(4-methylphenyl)benzoylamino]benzoyl}-1,2,3,4-tetrahydroquinoxalin-2-one (77.0 mg) as a white powder.
NMR ($CDCl_3$, δ) : 2.32 (3H, s), 2.34 (3H, s), 2.43 (2H, t, J=5Hz), 2.51 (2H, t, J=5Hz), 3.58-3.70 (4H, m), 4.62 (2H, s), 4.77 (2H, s), 6.68-6.88 (2H, m), 7.00-7.58 (14H, m), 7.86 (1H, dd, J=1, 8Hz)

Example 5

[0276] A mixture of 5-{4-[2-(2-methylphenyl)benzoylamino]-benzoyl}-1-(4-phthaloylaminobutyl)-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (800 mg) and hydrazin monohydrate (296 mg) in ethanol (20 ml) was stirred at ambient temperature for 6 hours. After removal of insoluble material by filtration, the filtrate was evaporated in vacuo and the residue was subjected to a silica gel column (20 g, 2% methanol in chloroform) to give 1-(4-aminobutyl)-5-{4-[2-(2-methylphenyl)benzoylamino]-benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (434 mg) as a pale yellow amorphous.
NMR ($CDCl_3$, δ) : 1.33-1.59 (4H, m), 1.67-1.85 (2H, m), 2.06 and 2.09 (total 3H, s), 2.44-2.77 (4H, m), 3.71-3.87 (2H, m), 4.00 (1H, m), 4.65 (1H, m), 6.69 (1H, br), 6.81-6.95 (3H, m), 7.03-7.36 (9H, m), 7.40-7.60 (2H, m), 8.07 (1H, dd, J=8, 1Hz)

Example 6

[0277] The following compounds were obtained according to a similar manner to that of Example 5.

1) 1-(3-Aminopropyl)-4-{4-[2-(4-methylphenyl)benzoylamino]benzoyl}-1,2,3,4-tetrahydroguinoxalin-2-one
NMR ($CDCl_3$ + CD_3OD, δ) : 2.00 (2H, tt, J=7.5, 7.5Hz), 2.35 (3H, s), 2.86 (2H, t, J=7.5Hz), 3.41 (3H, s), 4.12 (2H, t, J=7.5Hz), 4.55 (2H, s), 6.72-6.90 (2H, m), 7.17-7.58 (12H, m), 7.73-7.84 (2H, m), 8.21 (1H, m)

2) 1-{[4-(3-Aminopropyl)-1-piperazinyl]carbonylmethyl}-5-{4-[2-(4-methylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

Rf : 0.13 (10% methanol in chloroform)

FAB-MASS (m/z) : 659 (M^++1)

3) 1-(6-Aminohexyl)-5-{4-[2-(4-methylphenyl)-benzoylamino)benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

[0278] This product was used for next step without purification.

Example 7

[0279] A solution of 1-[4-[2-(2-azidomethylphenyl)-benzoylamino]benzoyl}-1,2,3,4-tetrahydroquinoline (535 mg) in a mixture of methanol (35 ml) and dioxane (4 ml) containing catalytic palladium on carbon (60 mg) was stirred under atmospheric pressure of hydrogen at ambient temperature. After 3 hours, the reaction mixture was filtered through a bed of celite, and then concentrated to give 1-{4-[2-(2-aminomethylphenyl)benzoylamino]benzoyl}-1,2,3,4-tetrahydroquinoline (395 mg) which was purified by recrystallization from a mixture of ethyl acetate and diethyl ether.

NMR ($CDCl_3$, δ) : 1.68 (2H, br s), 2.01 (2H, tt, J=7, 7Hz), 2.80 (2H, t, J=7Hz), 3.77 (1H, d, J=13Hz), 3.85 (2H, t, J=7Hz), 4.04 (1H, d, J=13Hz), 6.71 (1H, d, J=8Hz), 6.87 (1H, dd, J=8, 8Hz), 6.98 (1H, dd, J=8, 8Hz), 7.05-7.37 (11H, m), 7.40-7.59 (2H, m), 7.73-7.87 (1H, m)

Example 8

[0280] To a solution of 1-{4-[2-(2-aminomethylphenyl)-benzoylamino]benzoyl}-1,2,3,4-tetrahydroquinoline (100 mg) in dichloromethane (5 ml) were added pyridine (45 mg), acetic anhydride (23 μl) and catalytic amount of 4-dimethylaminopyridine. The reaction mixture was stirred for 1 hour at ambient temperature and washed with water and brine and the organic phase was dried over magnesium sulfate. The solvent was evaporated in vacuo and the residue was triturated with diethyl ether to give 1-{4-{2-(2-acetylaminomethyl)benzoylamino]benzoyl}-1,2,3,4-tetrahydroquinoline (90 mg).

NMR ($CDCl_3$, δ) : 1.81 (3H, s), 2.02 (2H, tt, J=7, 7Hz), 2.83 (2H, t, J=7Hz), 3.86 (2H, dt, J=3, 7Hz), 4.20 (1H, dd, J=15, 6Hz), 4.32 (1H, dd, J=15, 6Hz), 6.55-6.76 (2H, m), 6.87 (1H, dd, J=8, 8Hz), 6.98 (1H, dd, J=8, 8Hz), 7.06-7.65 (12H, m), 7.73-7.86 (1H, m), 8.30 (1H, br s)

Example 9

[0281] To a solution of 1-{4-[2-(2-aminomethylphenyl)-benzoylamino]benzoyl}-1,2,3,4-tetrahydroquinoline (180 mg), 37% formaldehyde (75 μl) and methanol (5 ml) containing acetic acid (0.1 ml) was added sodium cyanoborohydride (54 mg). The resulting mixture was stirred for 5 hours at ambient temperature and added sodium bicarbonate aqueous solution. The solution was evaporated and the residue was extracted with ethyl acetate and washed with brine, dried over sodium sulfate.. The solvent was evaporated in vacuo and triturated with diethyl ether to give 1-{4-[2-(2-dimethylaminomethylphenyl)benzoylamino]benzoyl}-1,2,3,4-tetrahydroquinoline (90 mg).

NMR ($CDCl_3$, δ) : 1.96 (6H, s), 2.00 (2H, tt, J=7, 7Hz), 2.81 (2H, t, J=7Hz), 2.85 (1H, d, J=13Hz), 3.84 (2H, t, J=7Hz), 3.88 (1H, d, J=13Hz), 6.75 (1H, d, J=8Hz), 6.82-7.05 (2H, m), 7.73-7.87 (1H, m), 10.10 (1H, br s)

Example 10

[0282] The following compounds were obtained according to a similar manner to that of Example 9.

1) 1-(4-Dimethylaminobutyl)-5-{4-[2-(2-methylphenyl)-benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 1.59 (2H, m), 1.68 (2H, m), 2.05 and 2.07 (total 3H, s), 2.28 (6H, s), 2.38 (2H, t, J=7Hz), 2.48-2.70 (2H, m), 3.72-4.03 (3H, m), 4.63 (1H, m), 6.71 (1H, br), 6.86 (2H, d, J=8.5Hz), 6.93 (1H, m), 7.05-7.16 (3H, m), 7.21-7.38 (7H, m), 7.46-7.59 (2H, m), 8.07 (1H, d, J=8Hz)

2) 1-(3-Dimethylaminopropyl-4-{4-[2-(4-methylphenyl)-benzoylamino]benzoyl}-1,2,3,4-tetrahydroquinoxalin-2-one

NMR ($CDCl_3$, δ) : 1.86 (2H, tt, J=7.5, 7.5Hz), 2.22 (6H, s), 2.36 (3H, s), 2.39 (2H, t, J=7.5Hz), 4.05 (2H, t, J=7.5Hz), 4.54 (2H, s), 6.69-6.87 (2H, m), 7.01-7.57 (14H, m), 7.86 (1H, d, J=8Hz)

3) 1-(6-Dimethylaminohexyl)-5-{4-[2-(4-methylphenyl)-benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 1.29-1.55 (6H, m), 1.60-1.81 (2H, m), 2.20-2.37 (2H, m), 2.21 (6H, s), 2.35 (3H, s), 2.49-2.74 (2H, m), 3.71-3.86 (2H, m), 4.01 (1H, m), 4.65 (1H, m), 6.22 (1H, d, J=7.5Hz), 6.91-7.03 (3H, m), 7.08-7.57 (12H, m), 7.82 (1H, dd, J=1.5, 7.5Hz)

Example 11

[0283] To a solution of 1-{4-[4-methoxy-2-(4-methylphenyl)-benzoylamino]benzoyl}-1,2,3,4-tetrahydroquinoline (380 mg) in dichloromethane (15 ml) at -78°C was added a solution of 1.0 M boron tribromide in dichloromethane (2.4 ml). The resulting solution was allowed to warm to ambient temperature where it was maintained for 12 hours. The mixture was cooled to 0°C, and added water. The organic layer was washed with saturated sodium bicarbonate aqueous solution and filtered through a bed of celite, and concentrated. The residue was triturated with diethyl ether to give 1-{4-[4-hydroxy-2-(4-methylphenyl)-benzoylamino]benzoyl}-1,2,3,4-tetrahydroquinoline (30 mg).

NMR ($CDCl_3$, δ) : 2.02 (2H, tt, J=7, 7Hz), 2.36 (3H, s), 2.82 (2H, t, J=7Hz), 3.88 (2H, t, J=7Hz), 6.49 (1H, br s), 6.68 (1H, d, J=8Hz), 6.77-6.93 (3H, m), 6.92-7.06 (4H, m), 7.09-7.35 (7H, m), 7.78 (1H, d, J=8Hz)

Example 12

[0284] The mixture of 1-ethoxycarbonylmethyl-5-{4-[2-(4-methylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (240 mg), 1N sodium hydroxide aqueous solution (2 ml) and ethanol (5 ml) was stirred for 1 hour at ambient temperature. The reaction was quenched with 1N hydrochloric acid (2 ml) and ethanol was removed. The residue was diluted with ethyl acetate and the solution was washed with brine, and the solution was dried over magnesium sulfate. Filtering and the removal of solvents afforded a crude product. The crude product was triturated with a mixture of diisopropyl ether and diethyl ether (1:1) to give 1-carboxymethyl-5-{4-[2-(4-methylphenyl) benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (217 mg) as a white powder.

mp : 175-183°C

NMR ($CDCl_3$, δ) : 2.36 (3H, s), 2.52-2.82 (2H, m), 3.82 (1H, dd, J=6, 13Hz), 4.42 (1H, d, J=17Hz), 4.55-4.86 (2H, m), 6.65-6.80 (1H, m), 6.90-7.58 (14H, m), 7.75 (1H, d, J=8Hz)

Example 13

[0285] The following compounds were obtained according to a similar manner to that of Example 12.

1) 1-Carboxymethyl-5-{4-[2-(2-methylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

mp : 200-205°C

NMR ($CDCl_3$, δ) : 2.10 (3H, s), 2.58-2.85 (2H, m), 3.80 (1H, dd, J=5, 11Hz), 4.38 (1H, d, J=17Hz), 4.60-4.90 (3H, m), 6.65-6.75 (1H, br s), 6.80-7.60 (14H, m), 8.00 (1H, d, J=8Hz)

2) 1-Carboxymethyl-5-{4-[2-(2,4-dimethylphenyl)-benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.00 and 2.04 (total 3H; s), 2.35 (3H, s), 2.54-2.86 (2H, m), 3.80 (1H, m), 4.32 (1H, d, J=17.5Hz), 4.68 (1H, m), 4.82 (1H, d, J=17.5Hz), 6.28 (2H, br), 6.72 (1H, m), 6.87 (2H, d, J=8.5Hz), 6.95 (1H, m), 7.02-7.39 (8H, m), 7.42-7.58 (2H, m), 7.99 (1H, d, J=8Hz)

3) 1-(2-Carboxyethyl)-5-{4-[2-(2-methylphenyl)-benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.08 (3H, br s), 2.42-2.76 (2H, m), 2.78-3.01 (2H, m), 3.70-4.83 (4H, m), 6.63-7.68 (16H, m), 8.05 (1H, br d, J=9Hz)

4) 1-(3-carboxypropyl)-5-{4-[2-(2-methylphenyl)-benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 1.68-2.80 (9H, m), 3.60-4.16 (3H, m), 4.45-4.80 (1H, m), 6.60-7.65 (16H, m), 8.06 (1H, br d, J=9Hz)

5) 1-(1-Carboxyethyl)-5-{4-[2-(2-methylphenyl)-benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 1.56-1.80 (3H, m), 1.96-2.15 (3H, m), 2.51-2.78 (2H, m), 3.65-5.04 (3H, m), 6.00-7.68 (16H, m), 7.95-8.15 (1H, m)

6) 1-Carboxymethyl-7,8-dimethyl-5-{4-[2-(4-methylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 1.99 (3H, s), 2.20 (3H, s), 2.34 (3H, s), 2.48-2.79 (2H, m), 3.55-3.80 (1H, m), 4.39 (1H, d, J=18Hz), 4.52-4.75 (1H, m), 4.68 (1H, d, J=18Hz), 6.43-6.52 (1H, br), 7.01 (3H, s), 7.08-7.57 (10H, m), 7.78 (1H, d, J=8Hz)

7) 1-Carboxymethyl-7-methyl-5-{4-[2-(4-methylphenyl)-benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.10 (3H, s), 2.35 (3H, s), 2.50-2.75 (2H, m), 3.15-3.34 (1H, br), 3.78 (1H, dd, J=5, 13Hz), 4.38 (1H, d, J=16Hz), 4.54-4.72 (1H, m), 4.70 (1H, d, J=16Hz), 6.49-6.58 (1H, br s), 6.95-7.32 (10H, m), 7.36-7.56 (3H, m), 7.77 (1H, d, J=8Hz)

8) 1-Carboxymethyl-8-chloro-5-{4-[2-(4-methylphenyl)-benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.39 (3H, s), 2.55-2.76 (2H, m), 3.79 (1H, dd, J=5, 13Hz), 4.42 (1H, d, J=17Hz), 4.52-4.73 (1H, m), 4.67 (1H, d, J=17Hz), 6.63-6.73 (1H, m), 6.92-7.33 (10H, m), 7.35-7.55 (3H, m), 7.78 (1H, d, J=7Hz)

9) 1-Carboxymethyl-8-chloro-5-{3-methyl-4-[2-(4-methylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

Rf : 0.75 (chloroform:methanol:acetic acid = 8:2:1)

10) 1-Carboxymethyl-8-chloro-5-{3-methoxy-4-[2-(4-methylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

Rf : 0.06 (10% methanol in chloroform)

11) 1-Carboxymethyl-5-{3-methoxy-4-[2-(4-methylphenyl)-benzoylamino]benzoyl}-8-methyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.32 (3H, s), 2.33 (3H, s), 2.55-2.80 (2H, m), 3.47 (3H, s), 3.80 (1H, dd, J=5, 13Hz), 4.29 (1H, d, J=18Hz), 4.58-4.78 (1H, m), 4.82 (1H, d, J=18Hz), 6.54-6.68 (2H, m), 6.79 (1H, d, J=8Hz), 6.90 (1H, s), 7.07 (1H, s), 7.15 (2H, d, J=8Hz), 7.25-7.59 (4H, m), 7.74-7.83 (2H, m), 8.18 (1H, d, J=9Hz)

12) 1-Carboxymethyl-8-methyl-5-{4-[2-(4-methylphenyl)-benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.36 (3H, s), 2.39 (3H, s), 2.55-2.86 (2H, m), 3.70-3.85 (1H, m), 4.40 (1H, d, J=17Hz), 4.56-4.76 (1H, m), 4.73 (1H, d, J=17Hz), 6.55-6.67 (1H, m), 6.74-6.82 (1H, m), 6.95-7.54 (12H, m), 7.79 (1H, d, J=7Hz)

13) 1-Carboxymethyl-8-methyl-5-{3-methyl-4-[2-(4-methylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

Rf : 0.06 (10% methanol in chloroform) 0.79 (chloroform:methanol:acetic acid = 8:2:1)

14) 1-carboxymethyl-8-methoxy-5-{4-[2-(4-methylphenyl)-benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.36 (3H, s), 2.53-2.79 (2H, m), 3.05-3.25 (1H, m), 3.68-3.84 (1H, m), 3.78 (3H, s), 4.38 (1H, d, J=17Hz), 4.55-4.78 (1H, m), 4.70 (1H, d, J=17Hz), 6.46-6.70 (2H, m), 6.78 (1H, m), 6.95-7.54 (11H, m), 7.78 (1H, d, J=7Hz)

15) 1-Carboxymethyl-5-{3-chloro-4-[2-(2-methylphenyl)-benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.13 and 2.15 (total 3H, s), 2.56-2.90 (2H, m), 3.75-3.92 (1H, m), 4.32 (1H, d, J=17Hz), 4.69 (1H, dt, J=5, 13Hz), 4.87 (1H, d, J=17Hz), 6.67-6.84 (1H, m), 6.86-7.12 (2H, m), 7.16-7.40 (7H, m), 7.42-7.63 (3H, m), 7.68 (1H, br s), 7.94 (1H, d, J=8Hz), 8.10-8.45 (2H, m)

16) 1-Carboxymethyl-5-{3-chloro-4-[2-(2,4-dimethylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1, 5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.07 and 2.15 (total 3H, s), 2.32 (3H, s), 2.55-2.90 (2H, m), 3.75-3.92 (1H, m), 4.32 (1H, d, J=17Hz), 4.58-4.80 (1H, m), 4.88 (1H, d, J=17Hz), 6.68-6.85 (1H, m), 6.86-7.48 (8H, m), 7.50-7.62 (2H, m), 7.74 (1H, br s), 7.88-8.00 (2H, m), 8.20-8.36 (1H, m)

17) 1-Carboxymethyl-5-{2-chloro-4-[2-(2,4-dimethylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 1.99 and 2.05 (total 3H, s), 2.40 (3H, s), 2.52-2.88 (2H, m), 3.69-3.88 (1H, m), 3.97-4.16 (1H, m), 4.85 (1H, d, J=16Hz), 4.77-4.98 (1H, m), 6.39-7.68 (15H, m), 7.96-8.12 (1H, m)

18) 1-Carboxymethyl-5-{4-[2-(2-methylphenyl)-benzoylamino]-3-nitrobenzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.17 and 2.22 (total 3H, s), 2.56-2.92 (2H, m), 3.77-3.95 (1H, m), 4.46 (1H, d, J=16Hz), 4.62-4.85 (1H, m), 4.82 (1H, d, J=16Hz), 6.65-6.82 (1H, m), 6.93-7.68 (11H, m), 7.74-7.90 (2H, m), 8.60 (1H, d, J=9Hz), 10.03 (1H, br s)

19) 1-Carboxymethyl-5-{4-[2-(2,4-dimethylphenyl)-benzoylamino)-2-nitrobenzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.00 and 2.02 (total 3H, s), 2.52-2.86 (2H, m), 3.72-3.90 (1H, m), 4.13-4.30 (1H, m), 4.80 (1H, d, J=16Hz), 4.76-5.00 (1H, m), 6.85-7.63 (15H, m), 8.01 (1H, d, J=9Hz)

20) 1-Carboxymethyl-5-{3-methoxy-4-[2-(4-methylphenyl)-benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.34 (3H, s), 2.55-2.91 (2H, m), 3.42 (3H, s), 3.76-3.95 (1H, m), 4.30 (1H, d, J=16Hz), 4.60-4.82 (1H, m), 4.84 (1H, d, J=16Hz), 6.58-7.08 (3H, m), 7.10-7.60 (10H, m), 7.71-7.87 (2H, m), 8.19 (1H, d, J=9Hz)

21) 1-Carboxymethyl-5-{3-methoxy-4-[2-(2-methylphenyl)-benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.07 and 2.12 (total 3H, s), 2.53-2.88 (2H, m), 3.47 (3H, s), 3.75-3.94 (1H, m), 4.27 (1H, d, J=16Hz), 4.59-4.80 (1H, m), 4.84 (1H, d, J=16Hz), 6.50-7.06 (4H, m), 7.12-7.67 (10H, m), 7.84 (1H, br s), 7.96 (1H, d, J=9Hz), 8.20 (1H, d, J=9Hz)

22) 1-Carboxymethyl-5-{3-methoxy-4-[2-(2,4-dimethylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.04 and 2.09 (total 3H, s), 2.33 (3H, s), 2.56-2.92 (2H, m), 3.47 (3H, s), 3.76-3.94 (1H, m), 4.28 (1H, d, J=16Hz), 4.60-4.84 (1H, m), 4.86 (1H, d, J=16Hz), 6.51-6.70 (1H, m), 6.71-6.94 (2H, m), 6.94-7.40 (6H, m), 7.40-7.65 (3H, m), 7.90 (1H, br s), 7.97 (1H, d, J=9Hz), 8.22 (1H, d, J=9Hz)

23) 1-carboxymethyl-5-{4-[2-(2,6-dimethylphenyl)-benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

Rf : 0.08 (10% methanol in chloroform)
0.75 (chloroform:methanol:acetic acid = 8:1:1)

24) 1-Carboxymethyl-5-{3-hydroxy-4-[2-(4-methylphenyl)-benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.09 (3H, s), 2.33 (2H, s), 2.43-2.60 (1H, m), 2.62-2.78 (1H, m), 3.69-3.84 (1H, m), 4.34-4.49 (1H, m), 6.52-7.81 (16H, m)

25) 1-Carboxymethyl-4,4-dimethyl-5-{4-[2-(4-methylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

Rf : 0.06 (10% methanol in chloroform)

26) 1-carboxymethyl-4-methyl-5-{4-[2-(4-methylphenyl)-benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

Rf : 0.09 (10% methanol in chloroform)

27) 1-[(4-Carboxymethyl-1-piperazinyl)carbonylmethyl]-5-{4-[2-(4-methylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR (DMSO-d_6, δ) : 2.28 (3H, s), 2.43-2.63 (6H, m), 3.20-3.60 (7H, m), 3.70-3.78 (1H, m), 4.45 (1H, d, J=17Hz), 5.00 (1H, d, J=17Hz), 6.80 (1H, d, J=6Hz), 6.96-7.02 (1H, m), 7.12 (4H, d, J=8Hz), 7.26 (4H, d, J=8Hz), 7.35-7.57 (6H, m)

28) 1-carboxymethyl-5-{4-[2-(4-methylphenyl)-benzoylamino)benzoyl}-8-trifluoromethyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

Rf : 0.10 (10% methanol in chloroform)

29) 1-Carboxymethyl-5-{2-methoxy-4-[2-(4-methylphenyl)-benzoylamino)benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.30 (3x3/4H, s), 2.34 (3x1/4H, s), 2.53-2.75 (2H, m), 3.70 (3H, s), 3.70-4.40 (2H, m), 4.87 (2H, m), 6.19 (1H, d, J=7.5Hz), 6.72-7.02 (3H, m), 7.10-7.57 (11H, m), 7.78 (1H, d, J=7.5Hz)

30) 1-Carboxymethyl-5-{6-[2-(4-methylphenyl)-benzoylamino]nicotinoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.29 (3H, s), 2.52-2.82 (2H, m), 3.75-3.89 (1H, m), 4.41-4.78 (3H, m), 6.74 (1H, d, J=7.5Hz), 7.01 (1H, dt, J=7.5, 1.5Hz), 7.12 (2H, d, J=8.5Hz), 7.18-7.51 (7H, m), 7.57-7.18 (2H, m), 7.90 (1H, d, J=1.5Hz), 8.09 (1H, d, J=7.5Hz), 8.82 (1H, br)

31) 1-carboxymethyl-5-{4-[2-(3-methylphenyl)-benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.27 (3H, s), 2.50-2.82 (2H, m), 3.80 (1H, dd, J=6, 12.5Hz), 4.38 (1H, d, J=17.7Hz), 4.53-4.81 (2H, m), 5.48 (1H, br), 6.71 (1H, d, J=7.5Hz), 6.96 (2H, d, J=8.5Hz), 7.03-7.29 (10H, m), 7.34-7.53 (3H, m), 7.87 (1H, d, J=7.5Hz)

32) 1-Carboxymethyl-7,8-dimethyl-5-{4-[2-(2,6-dimethylphenyl)benzoylamino]benzoyl}-1,3,4,5 tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 1.98 (3H, s), 2.01 (3H, s), 2.03 (3H, s), 2.20 (3H, s), 2.45-2.82 (2H, m), 3.72 (1H, m), 4.18 (1H, d, J=15Hz), 4.65 (1H, m), 4.72 (1H, d, J=15Hz), 6.85 (2H, d, J=8.5Hz), 6.98 (1H, s), 7.05-7.41 (7H, m), 7.48 (1H, s), 7.48-7.60 (2H, m), 8.21 (1H, dd, J=1.5, 7.5Hz)

33) 1-carboxymethyl-5-{4-[2-(4-methylphenyl)-benzoylamino]benzoyl}-2,3,4,5-tertrahydro-1H-1,5-benzodiazepine

NMR ($CDCl_3$ + CD_3OD, δ) : 1.95 (1H, m), 2.10 (1H, m), 2.34 (3H, s), 3.06-3.27 (2H, m), 3.65 (1H, m), 3.92 (1H, d, J=17.5Hz), 4.10 (1H, d, J=17.5Hz), 4.51 (1H, m), 6.51 (2H, m), 6.80 (1H, d, J=7.5Hz), 7.01-7.31 (10H, m), 7.39-7.55 (3H, m), 7.65 (1H, dd, J=1.5, 7.5Hz)

34) 1-Carboxymethyl-5-{4-[2-(2,6-dimethylphenyl)-benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.05 (3H, s), 2.20 (3H, s), 2.48-2.83 (2H, m), 3.71 (1H, m), 4.15 (1H, d, J=15Hz), 4.65 (1H, m), 4.74 (1H, d, J=15Hz), 6.86 (2H, d, J=8.5Hz), 6.96 (1H, s), 7.02-7.48 (7H, m), 7.51 (1H, s), 7.45-7.62 (2H, m), 8.24 (1H, dd, J=1.5, 7.5Hz)

35) 1-Carboxymethyl-5-{4-[N-2-(4-methylphenyl)benzoyl-N-methyl]aminobenzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.39 (3H, s), 2.55-2.82 (2H, m), 3.10 (3H, s), 3.79 (1H, m), 4.28 (1H, d, J=17Hz), 4.66 (1H, m), 4.82 (1H, d, J=17Hz), 6.01 (2H, d, J=8.5Hz), 6.63-6.85 (4H, m), 6.94-7.09 (4H, m), 7.20-7.34 (5H, m), 7.48 (1H, m)

36) 1-Carboxymethyl-5-{4-[2-(2-trifluoromethylphenyl)-benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.50-2.80 (2H, m), 3.76 (1H, m), 4.40 (1H, dd, J=4.5, 17.5Hz), 4.59 (1H, m), 4.70 (1H, d, J=17.5Hz), 5.74 (2H, br), 6.72 (1H, m), 6.96 (1H, m), 7.02-7.13 (3H, m), 7.20-7.34 (5H, m), 7.43-7.56 (4H, m), 7.64-7.73 (3H, m)

37) 1-Carboxymethyl-5-{4-[2-(2,4,6-trimethylphenyl)-benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 1.94 (3H, s), 1.99 (3H, 5), 2.37 (3H, s), 2.53-2.90 (2H, m), 3.80 (1H, m), 4.39 (1H, d,

J=17Hz), 4.57-4.96 (2H, m), 6.72 (1H, d, J=7.5Hz), 6.87 (1H, d, J=8.5Hz), 6.92-7.17 (5H, m), 7.27 (1H, s), 7.29 (2H, d, J=8.5Hz), 7.32-7.60 (3H, m), 8.21 (1H, m)

38) 1-Carboxymethyl-5-{3-methyl-4-[2-(4-methylphenyl)-benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 1.45 (3H, s), 2.37 (3H, s), 2.52-2.86 (2H, m), 3.82 (1H, m), 4.20 (1H, d, J=17Hz), 4.70 (1H, m), 4.83 (1H, d, J=17Hz), 6.69-5.85 (3H, m), 6.95 (1H, m), 7.09-7.56 (9H, m), 7.83 (1H, dd, J=1.5, 7.5Hz), 8.00 (1H, d, J=7.5Hz)

39) 5-Carboxymethyl-7-chloro-2-{4-[2-(4-methylphenyl)-benzoylamino]benzoyl}-2,3,4,5-tetrahydro-lH-1-benzazepine

NMR ($CDCl_3$, δ) : 2.33 (3H, s), 2.29 (1H, dd, J=6, 17.5Hz), 3.00 (1H, dd, J=6, 17.5Hz), 1.25-4.50 (7H, m), 6.53 (1H, d, J=7.5Hz), 6.87-7.01 (4H, m), 7.18-7.52 (10H, m), 7.74 (1H, d, J=7.5Hz)

40) 5-Carboxymethyl-1-{4-[2-(4-methylphenyl)benzoylamino]benzoyl}-2,3,4,5-tetrahydro-1H-1-benzazepine

NMR ($CDCl_3$, δ) : 1.35 (1H, m), 1.78-2.05 (2H, m), 2.35 (3H, s), 2.64-3.80 (5H, m), 4.51 (1H, m), 6.60 (1H, d, J=7.5Hz), 6.84-6.98 (4H, m), 7.10-7.55 (11H, m), 7.82 (1H, d, J=7.5Hz)

41) 5-Carboxymethyl-1-{4-[2-(2-methylphenyl)benzoylamino]benzoyl}-2,3,4,5-tetrahydro-1H-1-benzazepine

NMR ($CDCl_3$, δ) : 2.06 (3H, s), 2.73-3.10 (2H, m), 1.25-4.55 (7H, m), 6.59 (1H, d, J=7.5Hz), 6.82 (2H, d, J=8.5Hz), 6.92 (1H, m), 7.03-7.40 (10H, m), 7.44-7.58 (2H, m), 8.02 (1H, d, J=7.5Hz)

42) 5-Carboxymethyl-1-{4-[2-(4-methylphenyl)benzoylamino]benzoyl}-2,3-dihydro-1H-1-benzazepine

NMR ($CDCl_3$, δ) : 2.31 (3H, s), 2.37 (1H, m), 2.55 (1H, m), 3.36 (1H, m), 3.44 (1H, d, J=17.5Hz), 3.84 (1H, d, J=17.5Hz), 4.70 (1H, m), 6.20 (1H, t, J=5Hz), 6.59 (1H, d, J=7.5Hz), 6.79-6.94 (3H, m), 7.02-7.54 (12H, m), 7.54 (1H, d, J=7.5Hz)

Example 14

[0286] A solution of 1-(t-Butoxycarbonylmethyl)-4-{4-[2-(4-methylphenyl)benzoylamino]benzoyl}-1,2,3,4-tetrahydroquinoxalin-2-one (370 mg) in aqueous trifluoroacetic acid (15 ml) was stirred at ambient temperature for 2 hours and the solvent was evaporated in vacuo. The residue was dissolved in chloroform and the solution was washed with water and brine, and dried over magnesium sulfate. The solvent was evaporated in vacuo and the residue was purified by silica gel column (2% methanol in chloroform). The solvent was evaporated in vacuo and the residue was solidified with diethyl ether to give 1-carboxymethyl-4-{4-[2-(4-methylphenyl)benzoylamino]benzoyl}-1,2,3,4-tetrahydroquinoxalin-2-one (283 mg) as a white powder.

NMR ($CDCl_3$ + CD_3OD, δ) : 2.36 (3H, s), 4.60 (2H, s), 4.73 (2H, s), 6.70 (1H, d, J=8Hz), 6.82 (1H, t, J=8Hz), 6.97 (1H, d, J=8Hz), 7.10-7.57 (13H, m), 7.76 (1H, d, J=8Hz)

Example 15

[0287] To a solution of 1-carboxymethyl-5-{4-[2-(4-methylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (90 mg), N-methylpiperazine (17 mg) and 1-hydroxybenzotriazole (27 mg) in N,N-dimethylformamide (4 ml) was added 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (39 mg) at ambient temperature and the' mixture was stirred at the same temperature for 1.5 hours. The resulting mixture was diluted with ethyl acetate and then the solution was washed with saturated sodium bicarbonate aqueous solution and brine. Drying over magnesium sulfate, filtering and the removal of solvents afforded a crude product. The crude product was triturated with a mixture of diethyl ether and n-hexane (1:1) to give 5-{4-[2-(4-methylphenyl)benzoylamino]-benzoyl}-1-[(4-methyl-1-piperazinyl)carbonylmethyl]-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (100 mg) as a white powder.

mp : 161-163°C

NMR ($CDCl_3$, δ) : 2.35 (3H, s), 2.39 (3H, s), 2.40-2.95 (6H, m), 3.55-3.90 (5H, m), 4.10 (1H, d, J=16Hz), 4.71 (1H, dt, J=5, 10Hz), 5.18 (1H, d, J=16Hz), 6.72 (1H, d, J=8Hz), 6.88-7.60 (14H, m), 7.80 (1H, dd, J=1, 8Hz)

Example 16

[0288] The following compounds were obtained according to a similar manner to that of Example 15.

1) 5-{4-[2-(2-Methylphenyl)benzoylamino]benzoyl}-1-[(4-methyl-1-piperazinyl)carbonylmethyl]-1,3,4,5-tetrahy-

dro-1,5-benzodiazepin-2(2H)-one

mp : 150-154°C

NMR ($CDCl_3$, δ) : 2.07 and 2.10 (total 3H, s), 2.38 (3H, s), 2.40-2.68 (4H, m), 2.72-2.95 (1H, m), 3.56-3.88 (6H, m), 4.09 (1H, dd, J=1, 15Hz), 4.60-4.80 (1H, m), 5.18 (1H, dd, J=1, 15Hz), 6.65-6.75 (1H, br), 6.82-7.00 (3H, m), 7.06 (2H, d, J=8Hz), 7.17-7.40 (7H, m), 7.53 (2H, ddt, J=1, 9, 15Hz), 8.10 (1H, d, J=7Hz)

2) 1-(3-Dimethylpropylaminocarbonylmethyl)-5-{4-[2-(2-methylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

mp : 115-120°C

NMR ($CDCl_3$, δ) : 1.60-1.75 (2H, m), 2.08 (3H, s), 2.20 (3H, s), 2.38 (2H, t, J=6Hz), 2.55-2.80 (2H, m), 3.30-3.55 (2H, m), 3.80 (1H, dd, J=5, 13Hz), 4.03 (1H, d, J=16Hz), 4.60-4.80 (1H, m), 4.83 (1H, d, J=16Hz), 6.70 (1H, d, J=8Hz), 6.85 (2H, d, J=9Hz), 6.90-7.40 (8H, m), 7.48-7.62 (3H, m), 7.68-7.80 (1H, br), 8.10 (1H, dd, J=1, 8Hz)

3) 5-{4-[2-(2,4-Dimethylphenyl)benzoylamino]benzoyl}-1-[(4-methyl-1-piperazinyl)carbonylmethyl]-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 1.97 and 2.01 (total 3H, s), 2.33 (3H, s), 2.38 (3H, s), 2.42-2.56 (5H, m), 2.81 (1H, m), 3.56-3.87 (5H, m), 4.05 (1H, d, J=17.5Hz), 4.71 (1H, m), 5.69 (1H, d, J=17.5Hz), 6.69 (1H, br), 6.85 (1H, d, J=8.5Hz), 6.93 (1H, m), 7.02-7.26 (8H, m), 7.36 (1H, dd, J=8, 1Hz), 7.44-7.60 (2H, m), 8.06 (1H, d, J=8Hz)

4) 5-{4-[2-(2-Methylphenyl)benzoylamino]benzoyl}-1-[2-(4-methyl-1-piperazinyl)carbonylethyl]-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.08 (3H, br s), 2.30 (3H, s), 2.22-3.02 (8H, m), 3.40-3.90 (5H, m), 4.05-4.33 (2H, m), 4.52-4.82 (1H, m), 6.60-7.22 (5H, m), 7.23-7.67 (11H, m), 8.09 (1H, br d, J=9Hz)

5) 5-{4-[2-(2-Methylphenyl)benzoylamino]benzoyl}-1-{3-(4-methyl-1-piperazinyl)carbonylpropyl]-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 1.89-2.80 (13H, m), 2.28 (3H, s), 3.31-3.51 (2H, m), 3.51-3.68 (2H, m), 3.70-3.87 (1H, m), 3.88-4.10 (2H, m), 4.50-4.80 (1H, m), 6.53-7.66 (16H, m), 8.07 (1H, br d, J=9Hz)

6) 5-{4-[2-(2-Methylphenyl)benzoylamino]benzoyl}-1-[1-(4-methyl-1-piperazinyl)carbonylethyl]-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)one

NMR ($CDCl_3$, δ) : 1.24-1.43 (3H, m), 1.97-2.15 (3H, m), 2.36 (3H, s), 2.38-2.77 (6H, m), 3.43-4.06 (5H, m), 4.45-4.71 (1H, m), 5.64 (1H, q, J=8Hz), 6.56-7.67 (15H, m), 7.95-8.18 (2H, m)

7) 7,8-Dimethyl-5-{4-[2-(4-methylphenyl)benzoylamino]-benzoyl}-1-[(4-methyl-1-piperazinyl)carbonylmethyl]-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 1.98 (3H, s), 2.20 (3H, s), 2.36 (3H, s), 2.38 (3H, s), 2.40-2.63 (5H, m), 2.69-2.88 (1H, m), 3.55-3.83 (5H, m), 4.05 (1H, d, J=16Hz), 4.57-4.78 (1H, m), 5.10 (1H, d, J=16Hz), 6.41-6.47 (1H, br s), 6.99 (3H, d, J=8Hz), 7.09-7.36 (7H, m), 7.38-7.59 (3H, m), 7.83 (1H, dd, J=1, 7Hz)

8) 7-Methyl-5-{4-[2-(4-methylphenyl)benzoylamino]-benzoyl}-1-[(4-methyl-1-piperazinyl)carbonylmethyl]-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.09 (3H, s), 2.35 (3H, s), 2.38 (3H, s), 2.40-2.63 (5H, m), 2.72-2.90 (1H, m), 3.56-3.86 (5H, m), 4.06 (1H, d, J=16Hz), 4.60-4.78 (1H, m), 5.12 (1H, d, J=16Hz), 6.48-6.53 (1H, br s), 6.96-7.36 (11H, m), 7.38-7.59 (3H, m), 7.83 (1H, dd, J=1, 8Hz)

9) 8-Chloro-5-{4-[2-(4-methylphenyl)benzoylamino]-benzoyl}-1-[(4-methyl-1-piperazinyl)carbonylmethyl]-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.38 (3H, s), 2.39 (3H, s), 2.44-2.92 (6H, m), 3.58-3.87 (5H, m), 4.06 (1H, d, J=16Hz), 4.59-4.77 (1H, m), 5.03 (1H, d, J=16Hz), 6.65 (1H, d, J=9Hz), 6.89-7.35 (11H, m), 7.39-7.59 (3H, m), 7.83 (1H, dd, J=1, 8Hz)

10) 8-Chloro-5-{3-methyl-4-[2-(4-methylphenyl)benzoylamino]benzoyl}-1-[(4-methyl-1-piperazinyl)carbonylmethyl]-1,3,4,5-tetrahydro-1,5-benzodiazepine-2(2H)-one

NMR ($CDCl_3$, δ) : 1.46 (3H, s), 2.37 (6H, s), 2.42-2.90 (6H, m), 3.49-3.87 (5H, m), 4.05 (1H, d, J=15Hz), 4.59-4.78 (1H, m), 5.17 (1H, d, J=15Hz), 6.61-6.74 (2H, m), 6.89-6.98 (2H, m), 7.18-7.58 (8H, m), 7.84 (1H, dd, J=1, 8Hz), 8.08 (1H, d, J=8Hz)

11) 8-Chloro-5-{3-methoxy-4-[2-(4-methylphenyl)-benzoylamino]benzoyl}-1-[(4-methyl-1-piperazinyl)-carbonylmethyl]-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.38 (6H, s), 2.40-2.80 (6H, m), 3.50-3.88 (5H, m), 3.54 (3H, s), 4.06 (1H, d, J=15Hz), 4.58-4.76 (1H, m), 5.13 (1H, d, J=15Hz), 6.42 (1H, d, J=8Hz), 6.68 (1H, d, J=9Hz), 6.94 (1H, dd, J=1, 9Hz), 7.04 (1H, s), 7.17 (2H, d, J=8Hz), 7.26-7.59 (5H, m), 7.80 (2H, d, J=8Hz), 8.20 (1H, d, J=9Hz)

12) 5-{3-Methoxy-4-[2-(4-methylphenyl)benzoylamino]-benzoyl}-8-methyl-1-[(4-methyl-1-piperazinyl)-carbonylmethyl]-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.29 (3H, s), 2.36 (6H, s), 2.43-2.67 (5H, m), 2.73-2.92 (1H, m), 3.50-3.84 (5H, m), 3.57 (3H, s), 4.04 (1H, d, J=16Hz), 4.60-4.79 (1H, m), 5.14 (1H, d, J=16Hz), 6.39 (1H, d, J=8Hz), 6.60 (1H, d, J=8Hz), 6.75 (1H, d, J=8Hz), 7.08 (1H, d, J=1Hz), 7.16 (3H, d, J=6Hz), 7.25-7.32 (2H, m), 7.38-7.59 (3H, m), 7.77-7.82 (2H, m), 8.16 (1H, d, J=9Hz)

13) 5-{4-[2-(2,4-Dimethylphenyl)benzoylamino]-3-methoxybenzoyl}-8-methyl-1-[(4-methyl-1-piperazinyl)-carbonylmethyl]-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.03 and 2.13 (total 3H, s), 2.29 (3H, s), 2.32 (3H, s), 2.33 (3H, s), 2.43-2.66 (5H, m), 2.72-2.91 (1H, m), 3.50-3.86 (5H, m), 3.57 (3H, s), 4.03 (1H, d, J=15Hz), 4.59-4.78 (1H, m), 5.15 (1H, dd, J=5, 15Hz), 6.26-6.41 (1H, br), 6.58 (1H, d, J=8Hz), 6.72 (1H, d, J=8Hz), 6.99-7.26 (6H, m), 7.40-7.58 (2H, m), 7.88-7.95 (1H, br s), 7.94 (1H, dd, J=1, 6Hz), 8.08 (1H, d, J=8Hz)

14) 8-Methyl-5-{4-[2-(4-methylphenyl)benzoylamino]-benzoyl}-1-[(4-methyl-1-piperazinyl)carbonylmethyl]-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.30 (3H, s), 2.37 (3H, s), 2.39 (3H, s), 2.41-2.67 (5H, m), 2.70-2.91 (1H, m), 3.57-3.84 (5H, m), 4.06 (1H, d, J=16Hz), 4.60-4.79 (1H, m), 5.13 (1H, d, J=16Hz), 6.59 (1H, d, J=8Hz), 6.74 (1H, d, J=8Hz), 6.94-7.04 (3H, m), 7.07-7.35 (7H, m), 7.38-7.59 (3H, m), 7.82 (1H, dd, J=1, 7Hz)

15) 8-Methyl-5-{3-methyl-4-[2-(4-methylphenyl)benzoylamino]benzoyl}-1-[(4-methyl-1-piperazinyl)-carbonylmethyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 1.46 (3H, s), 2.30 (3H, s), 2.37 (6H, s), 2.40-2.68 (6H, m), 3.55-3.86 (5H, m), 4.06 (1H, d, J=15Hz), 4.60-4.78 (1H, m), 5.18 (1H, d, J=15Hz), 6.55-6.80 (3H, m), 6.90 (1H, s), 7.19 (3H, d, J=9Hz), 7.22-7.59 (5H, m), 7.82 (1H, dd, J=1, 8Hz), 8.02 (1H, d, J=9Hz)

16) 8-Methoxy-5-{4-[2-{4-methylphenyl)benzoylamino]-benzoyl}-1-[(4-methyl-1-piperazinyl)carbonylmethyl]-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.37 (3H, s), 2.39 (3H, s), 2.40-2.67 (5H, m), 2.73-2.92 (1H, m), 3.55-3.82 (5H, m), 3.78 (3H, s), 4.04 (1H, d, J=16Hz), 4.60-4.78 (1H, m), 5.15 (1H, d, J=16Hz), 6.48 (1H, d, J=8Hz), 6.60 (1H, d, J=8Hz), 6.92-7.13 (6H, m), 7.18-7.36 (4H, m), 7.38-7.58 (3H, m), 7.82 (1H, dd, J=1, 8Hz)

17) 5-{3-Chloro-4-[2-(2-methylphenyl)benzoylamino]-benzoyl}-1-[(4-methyl-1-piperazinyl)carbonylmethyl]-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.13 and 2.15 (total 3H, s), 2.36 (3H, s), 2.41-2.72 (5H, m), 2.84 (1H, dt, J=7, 14Hz), 3.48-3.91 (5H, m), 4.07 (1H, d, J=16Hz), 4.70 (1H, dt, J=7, 14Hz), 5.16 (1H, d, J=16Hz), 6.65-7.11 (3H, m), 7.16-7.64 (10H, m), 7.69 (1H, br s), 7.94 (1H, d, J=8Hz), 8.25 (1H, d, J=8Hz)

18) 5-{3-Chloro-4-[2-(2-methylphenyl)benzoylamino]-benzoyl}-1-[(4-dimethylamino-1-piperidyl)carbonylmethyl]-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 1.38-2.05 (4H, m), 2.11 and 2.14 (total 3H, s), 2.34 (6H, s), 2.30-2.52 (1H, m), 2.53-2.97 (3H, m), 3.01-3.34 (1H, m), 3.70-4.20 (3H, m), 4.56-4.80 (2H, m), 5.09-5.28 (1H, m), 6.64-7.04 (3H, m), 7.12-7.63 (10H, m), 7.69 (1H, br s), 7.93 (1H, d, J=8Hz), 8.25 (1H, d, J=8Hz)

19) 5-{3-Chloro-4-[2-(2,4-dimethylphenyl)benzoylamino]-benzoyl}-1-[(4-methyl-1-piperazinyl)carbonylmethyl]-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.06 and 2.12 (total 3H, s), 2.33 (3H, s), 2.36 (3H, s), 2.40-2.71 (5H, m), 2.83 (1H, dt, J=13, 6Hz), 3.48-3.90 (5H, m), 4.08 (1H, d, J=16Hz), 4.70 (1H, dt, J=13, 6Hz), 5.16 (1H, d, J=16Hz), 6.64-7.61 (12H, m), 7.69-7.80 (1H, m), 7.93 (1H, d, J=8Hz), 8.27 (1H, d, J=8Hz)

20) 5-{2-Chloro-4-[2-(2,4-dimethylphenyl)benzoylamino]-benzoyl}-1-[(4-methyl-1-piperazinyl)carbonylmethyl]-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 1.98 and 2.02 (total 3H, s), 2.36 (3H, s), 2.41 (3H, s), 2.27-2.70 (5H, m), 2.82 (1H, dt, J=7, 14Hz), 3.44-3.96 (6H, m), 4.89 (1H; dt, J=7, 14Hz), 5.16 (1H, d, J=16Hz), 6.62-7.03 (4H, m), 7.04-7.33 (8H, m), 7.43-7.63 (2H, m), 8.05 (1H, d, J=9Hz)

21) 5-{4-[2-(2-Methylphenyl)benzoylamino]-3-nitrobenzoyl}-1-[(4-methyl-1-piperazinyl)carbonylmethyl]-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.16 and 2.18 (total 3H, s), 2.36 (3H, s), 2.39-2.75 (5H, m), 2.87 (1H, dt, J=7, 14Hz), 3.48-3.95 (5H, m), 4.26 (1H, d, J=16Hz), 4.73 (1H, dt, J=7, 14Hz), 5.13 (1H, d, J=16Hz), 6.71 (1H, d, J=9Hz), 6.88-7.42 (8H, m), 7.43-7.69 (3H, m), 7.72-7.91 (2H, m), 8.63 (1H, d, J=9Hz), 10.02 (1H, s)

22) 5-{4-[2-(2,4-Dimethylphenyl)benzoylamino]-2-nitrobenzoyl}-1-[(4-methyl-1-piperazinyl)carbonylmethyl]-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.00 and 2.03 (total 3H, s), 2.36 (3H, s), 2.42 (3H, s), 2.30-2.70 (5H, m), 2.82 (1H, dt, J=6, 15Hz), 3.46-3.90 (5H, m), 3.95 (1H, d, J=16Hz), 4.94 (1H, dt, J=5,13Hz), 5.17 (1H, d, J=16Hz), 6.80-7.07 (2H, m), 7.11-7.72 (12H, m), 8.10 (1H, d, J=9Hz)

23) 5-{3-Methoxy-4-[2-(2-methylphenyl)benzoylamino]-benzoyl}-1-[(4-methyl-1-piperazinyl)carbonylmethyl]-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.09 and 2.16 (total 3H, s), 2.37 (3H, s), 2.40-2.72 (5H, m), 2.84 (1H, dt, J=7, 13Hz), 3.57 (3H, s), 3.51-3.91 (5H, m), 4.06 (1H, d, J=16Hz), 4.71 (1H, dt, J=7, 13Hz), 5.21 (1H, d, J=16Hz), 6.29-6.48 (1H, m), 6.65-6.78 (1H, m), 6.86-7.07 (2H, m), 7.14-7.33 (6H, m), 7.35 (1H, d, J=9Hz), 7.43-7.60 (2H, m), 7.85 (1H, br s), 7.95 (1H, d, J=9Hz), 8.16 (1H, d, J=9Hz)

24) 5-{3-Methoxy-4-[2-(4-methylphenyl)benzoylamino]-benzoyl}-1-[(4-methyl-1-piperazinyl)carbonylmethyl]-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.36 (6H, s), 2.41-2.72 (5H, m), 2.85 (1H, dt, J=7, 14Hz), 3.53 (3H, s), 3.55-3.92 (5H, m), 4.06 (1H, d, J=16Hz), 4.72 (1H, dt, J=5, 14Hz), 5.19 (1H, d, J=16Hz), 6.42 (1H, d, J=9Hz), 6.74 (1H, d, J=9Hz), 6.90-7.07 (2H, m), 7.11-7.22 (2H, m), 7.23-7.60 (7H, m), 7.73-7.86 (2H, m), 8.16 (1H, d, J=9Hz)

25) 1-[(4-Dimethylamino-1-piperidyl)carbonylmethyl]-5-{3-methoxy-4-[2-(2-methylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1, 5-benzodiazepin-2{2H)-one

NMR ($CDCl_3$, δ) : 1.36-2.20 (4H, m), 2.09 and 2.16 (total 3H, s), 2.34 (6H, s), 2.30-2.97 (10H, m), 3.02-3.32 (1H, m), 3.53 and 3.56 (total 3H, s), 3.66-4.18 (3H, m), 4.57-4.81 (2H, m), 5.07-5.31 (1H, m), 6.26-6.48 (1H, m), 6.64-6.78 (1H, m), 6.85-7.07 (2H, m), 7.08-7.41 (7H, m), 7.42-7.60 (2H, m), 7.85 (1H, br s), 7.95 (1H, d, J=9Hz), 8.15 (1H, d, J=9Hz)

26) 5-{3-Methoxy-4-[2-(2,4-dimethylphenyl)benzoylamino]-benzoyl}-1-[(4-methyl-1-piperazinyl)carbonylmethyl]-1,3,4,5-tetrahydro-1, 5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.03 and 2.12 (total 3H, s), 2.34 (3H, s), 2.36 (3H, s), 2.40-2.72 (5H, m), 2.73-2.96 (1H, m), 3.47-3.92 (5H, m), 3.56 (3H, s), 4.05 (1H, d, J=16Hz), 4.71 (1H, dt, J=5, 14Hz), 5.20 (1H, d, J=16Hz), 6.28-6.46 (1H, m), 6.65-6.79 (1H, m), 6.86-7.30 (7H, m), 7.36 (1H, d, J=9Hz), 7.40-7.58 (2H, m), 7.84-8.00 (2H, m), 8.18 (1H, d, J=9Hz)

27) 1-[(4-Dimethylamino-1-piperidyl)carbonylmethyl]-5-{3-methoxy-4-[2-(2,4-dimethylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 1.37-2.15 (4H, m) , 2.04 and 2.13 (total 3H, s), 2.34 (9H, s), 2.38-2.99 (4H, m), 3.04-3.32 (1H, m), 3.56 and 3.59 (total 3H, s), 3.72-4.19 (3H, m), 4.56-4.82 (2H, m), 5.09-5.30 (1H, m), 6.25-6.50 (1H, m), 6.64-6.70 (1H, m), 6.88-7.60 (10H, m), 7.83-8.02 (2H, m), 8.18 (1H, d, J=9Hz)

28) 1-[(4-Dimethylamino-1-piperidyl)carbonylmethyl]-5-{4-[2-(2,6-dimethylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 1.43-2.14 (4H, m), 1.99 (3H, s), 2.01 (3H, s), 2.32 (6H, s), 2.35-2.94 (4H, m), 3.04-3.31 (1H, m), 3.80 (1H, dd, J=5, 13Hz), 3.90-4.18 (2H, m), 4.57-4.80 (2H, m), 5.20 (1H, dd, J=10, 15Hz), 6.59 (1H, d, J=8Hz), 6.82-6.98 (3H, m), 7.03 (2H, d, J=9Hz), 7.12-7.40 (5H, m), 7.43-7.65 (3H, m), 8.26 (1H, dd, J=1, 8Hz)

29) 1-[(4-Dimethylamino-1-piperidyl)carbonylmethyl]-5-{4-[2-(2-methylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 1.40-1.70 (2H, m), 1.80-2.05 (2H, m), 2.08 (3H, d, J=7Hz), 2.30 (6H, s), 2.25-2.90 (4H, m),

3.05-3.32 (1H, m), 3.72 (1H, dd, J=5, 13Hz), 3.88-4.20 (2H, m), 4.55-4.70 (2H, m), 5.10-5.30 (1H, m), 6.60-6.75 (1H, br), 6.90 (2H, d, J=8Hz), 7.05 (2H, d, J=8Hz), 7.15-7.41 (8H, m), 7.55 (2H, ddd, J=1, 7, 14Hz), 8.08 (1H, d, J=7Hz)

30) 1-[(4-Dimethylamino-1-piperidyl)carbonylmethyl]-5-{4-[2-(4-methylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 1.42-1.73 (2H, m), 1.80-2.11 (2H, m), 2.28-2.50 (1H, m), 2.30 (6H, s), 2.38 (3H, s), 2.56-2.93 (3H, m), 3.05-3.30 (1H, m), 3.82 (1H, dd, J=5, 13Hz), 3.90-4.19 (2H, m), 4.58-4.80 (2H, m), 5.21 (1H, dd, J=10, 16Hz), 6.70 (1H, d, J=9Hz), 6.89-7.04 (4H, m), 7.09 (2H, d, J=8Hz), 7.15-7.60 (8H, m), 7.83 (1H, dd, J=1, 8Hz)

31) 5-{4-[2-(4-Methylphenyl)benzoylamino]benzoyl}-1-[(4-methyl-1-piperazinyl)carbonylmethyl]-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.30 and 2.32 (total 3H, s), 2.38 and 2.39 (total 3H, s), 2.52-2.91 (8H, m), 3.04-3.08 (2H, m), 3.82 (1H, dd, J=5, 12Hz), 4.09 (1H, d, J=17Hz), 4.60-4.80 (1H, m), 5.37 (1H, d, J=17Hz), 6.38-6.41 (1H, br s), 6.68-6.76 (1H, m), 6.90-7.07 (4H, m), 7.08-7.61 (10H, m), 7.82 (1H, dd, J=1, 8Hz)

32) 5-{3-Hydroxy-4-[2-(4-methylphenyl)benzoylamino]-benzoyl}-1-[(4-methyl-1-piperazinyl)carbonylmethyl]-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.32 (3H, s), 2.36 (3H, s), 2.20-2.66 (5H, m), 2.79 (1H, m), 3.50-3.88 (5H, m), 4.46 (1H, d, J=15Hz), 4.64 (1H, m), 4.96 (1H, d, J=15Hz), 6.62-6.84 (3H, m), 6.90-7.08 (2H, m), 7.09-7.60 (10H, m), 7.78 (1H, d, J=9Hz)

33) 4,4-Dimethyl-5-{4-[2-(4-methylphenyl)benzoylamino]-benzoyl}-1-[(4-methyl-1-piperazinyl)carbonylmethyl]-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 1.56 (3H, s), 1.62 (3H, s), 1.93 (3H, s), 2.20-2.60 (5H, m), 2.36 (3H, s), 2.70 (1H, d, J=13Hz), 3.60-3.83 (4H, m), 4.10 (1H, d, J=15Hz), 5.24 (1H, d, J=15Hz), 6.69 (1H, dd, J=1, 8Hz), 6.83-6.97 (4H, m), 7.04-7.32 (7H, m), 7.37-7.57 (3H, m), 7.80 (1H, dd, J=1, 8Hz)

34) 4-Methyl-5-{4-[2-(4-methylphenyl)benzoylamino]-benzoyl}-1-[(4-methyl-1-piperazinyl)carbonylmethyl]-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

Rf : 0.33 (10% methanol in chloroform)

NMR ($CDCl_3$, δ) : 1.27 (3H, d, J=6Hz), 2.38 (3H, s), 2.39 (3H, s), 2.40-2.64 (7H, m), 3.55-3.80 (4H, m), 3.98 (1H, d, J=16Hz), 5.13-5.30 (1H, br), 5.24 (1H, d, J=16Hz), 6.64-6.72 (1H, br), 6.92-7.02 (5H, m), 7.17-7.55 (8H, m), 7.80 (1H, d, J=8Hz)

35) 1-{[4-(2-Hydroxyethyl)-1-piperazinyl]carbonylmethyl}-5-{4-[2-(4-methylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

Rf : 0.19 (chloroform:methanol:acetic acid = 8:2:1) 0.21 (10% methanol in chloroform)

NMR ($CDCl_3$, δ): 2.40 (3H, s), 2.55-2.85 (8H, m), 3.60-3.88 (7H, m), 4.10 (1H, d, J=15Hz), 4.62-4.80 (1H, m), 5.16 (1H, d, J=15Hz), 6.73 (1H, d, J=8Hz), 6.90-7.15 (6H, m), 7.17-7.55 (8H, m), 7.82 (1H, dd, J=1, 8Hz)

36) 5-{4-[2-(4-Methylphenyl)benzoylamino]benzoyl}-1-{[4-(1-pyrrolidinylcarbonylmethyl)-1-piperazinyl]-carbonylmethyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 1.82-2.04 (4H, m), 2.38 (3H, s), 2.58-2.85 (6H, m), 3.20 (2H, s), 3.49 (4H, dd, J=8, 13Hz), 3.62-3.88 (5H, m), 4.10 (1H, d, J=16Hz), 4.63-4.80 (1H, m), 5.16 (1H, d, J=16Hz), 6.72 (1H, d, J=8Hz), 6.93-7.15 (4H, m), 7.18-7.58 (10H, m), 7.82 (1H, d, J=8Hz)

37) 1-{[4-(3,4-Methylenedioxybenzyl)-1-piperazinyl]-carbonylmethyl}-5-{4-[2-(4-methylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.37 (3H, s), 2.41-2.68 (5H, m), 2.74-2.85 (1H, m), 3.43-3.86 (8H, m), 4.08 (1H, d, J=16Hz), 4.62-4.79 (1H, m), 5.15 (1H, d, J=16Hz), 5.96 (2H, s), 6.68-6.78 (3H, m), 6.85-7.02 (5H, m), 7.08 (2H, d, J=9Hz), 7.17-7.58 (8H, m), 7.82 (1H, dd, J=1, 8Hz)

38) 5-{4-[2-(4-Methylphenyl)benzoylamino]benzoyl}-1-{[4-(2-pyridyl)-1-piperazinyl]carbonylmethyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.39 (3H, s), 2.63 (1H, dd, J=5, 14Hz), 2.78-2.87 (1H, m), 3.59-3.88 (9H, m), 4.14 (1H, d, J=15Hz), 4.65-4.78 (1H, m), 5.21 (1H, d, J=15Hz), 6.67-6.73 (3H, m), 6.95-7.02 (4H, m), 7.11 (2H, d, J=8Hz), 7.19-7.33 (4H, m), 7.38-7.58 (5H, m), 7.82 (1H, d, J=8Hz), 8.21-8.24 (1H, m)

39) 1-[(4-Methyl-1-homopiperazinyl)carbonylmethyl]-5-{4-[2-(4-methylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 1.92-2.11 (2H, m), 2.38 (3H, s), 2.42 and 2.44 (total 3H, s), 2.59-2.72 (4H, m), 2.77-2.89 (2H, m), 3.63-3.87 (5H, m), 4.02 (1H, dd, J=6, 15Hz), 4.64-4.78 (1H, m), 5.18 (1H, dd, J=2, 15Hz), 6.69-6.74 (1H, br), 6.92-7.01 (4H, m), 7.10 (2H, d, J=8Hz), 7.18-7.32 (5H, m), 7.39-7.57 (4H, m), 7.83 (1H, d, J=8Hz)

40) 1-[(4-tert-Butoxycarbonyl-1-piperazinyl)carbonylmethyl]-5-{4-[2-(4 methylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

Rf : 0.79 (10% methanol in chloroform)

41) 1-[(4-Ethoxycarbonylmethyl-1-piperazinyl)carbonylmethyl]-5-{4-[2-(4-methylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 1.31 (3H, t, J=8Hz), 2.38 (3H, s), 2.59-2.80 (6H, m), 3.28 (2H, s), 3.63-3.88 (5H, m), 4.17 (1H, d, J=15Hz), 4.21 (2H, dd, J=7, 15Hz), 4.62-4.81 (1K, m), 5.17 (1K, d, J=15Hz), 6.68-6.76 (1H, br), 6.93-7.02 (3H, m), 7.08-7.14 (2H, m), 7.18-7.59 (10H, m), 7.83 (1H, dd, J=1, 8Hz)

42) 5-{4-[2-(4-Methylphenyl)benzoylamino]benzoyl}-1-{[4-(3-phthalimidopropyl)-1-piperazinyl]carbonylmethyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 1.90 (2H, q, J=7Hz), 2.38 (3H, s), 2.40-2.67 (7H, m), 2.73-2.92 (1H, m), 3.40-3.58 (4H, m), 3.79-3.88 (3H, m), 4.02 (1H, d, J=15Hz), 4.62-4.79 (1H, m), 5.13 (1H, d, J=15Hz), 6.68-6.76 (1H, m), 6.95-7.15 (6H, m), 7.19-7.58 (9H, m), 7.70-7.79 (2H, m), 7.80-7.90 (3H, m)

43) 5-{4-[2-(4-Methylphenyl)benzoylamino]benzoyl}-1-[(4-methyl-1-piperazinyl)carbonylmethyl]-8-trifluoromethyl-1,3,4,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.37 (3H, s), 2.38 (3H, s), 2.42-2.78 (6H, m), 3.60-3.78 (4H, m), 3.80-3.92 (1H, m), 4.12 (1H, d, J=15Hz), 4.62-4.73 (1H, m), 5.15 (1H, d, J=15Hz), 6.86 (1H, d, J=8Hz), 6.98-7.06 (3H, m), 7.14 (2H, d, J=9Hz), 7.19-7.34 (4H, m), 7.39-7.57 (3H, s), 7.67 (1H, s), 7.84 (1H, d, J=8Hz)

44) 5-{2-Methoxy-4-[2-(4-methylphenyl)benzoylamino]-benzoyl}-1-(4-methyl-1-piperazinylcarbonyl)methyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.37 (3H, s), 2.38 (3H, s), 2.75-2.64 (6H, m), 2.80 (1H, m), 3.50-3.86 (5H, m), 3.69 (1H, s), 4.88 (1H, dt, J=5, 15Hz), 5.71 (1H, d, J=16Hz), 6.40 (1H, d, J=7.5Hz), 6.70-6.79 (1H, m), 6.85-6.94 (2H, m), 7.06-7.56 (11H, m), 7.82 (1H, d, J=7.5Hz)

45) 5-{6-[2-(4-Methylphenyl)benzoylamino]nicotinoyl}-1-(4-methyl-1-piperazinylcarbonyl)methyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.32 (3H, s), 2.35 (3H, s), 2.40-2.68 (5H, m), 2.83 (1H, m), 3.57 (2H, m), 3.71 (2H, m), 3.84 (1H, m), 4.18 (1H, d, J=16Hz), 4.72 (1H, dt, J=5, 13Hz), 5.07 (1H, d, J=16Hz), 6.72 (1H, d, J=7.5Hz), 6.98 (1H, m), 7.16 (2H, d, J=8.5Hz), 7.23-7.55 (9H, m), 7.70 (1H, m), 7.97 (1H, m), 8.05 (1H, d, J=7.5Hz)

46) 5-{4-[2-(3-Methylphenyl)benzoylamino]benzoyl}-1-(4-methyl-1-piperazinylcarbonyl)methyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.29 (3H, s), 2.36 (3H, s), 2.41-2.67 (5H, m), 2.82 (1H, m), 3.56-3.87 (5H, m), 4.07 (1H, d, J=16Hz), 4.71 (1H, dt, J=5, 13Hz), 5.70 (1H, d, J=16Hz), 6.69 (1H, d, J=7.5Hz), 6.88-7.00 (3H, m), 7.08 (2H, d, J=8.5Hz), 7.17-7.58 (10H, m), 7.86 (1H, m)

47) 7,8-Dimethyl-5-{4-[2-(2,6-dimethylphenyl)benzoylamino]benzoyl}-1-(4-methyl-1-piperazinylcarbonyl)-methyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 1.95 (3H, s), 1.99 (3H, s), 2.02 (3H, s), 2.19 (3H, s), 2.35 (3H, s), 2.43-2.61 (5H, m), 2.79 (1H, m), 3.50-3.86 (5H, m), 4.01 (1H, d, J=15.5Hz), 4.64 (1H, m), 5.13 (1H, d, J=15.5Hz), 6.44 (1H, br), 6.87 (2H, d, J=8.5Hz), 7.06-3.37 (6H, m), 7.54 (1H, s), 7.55-7.64 (2H, m), 8.28 (1H, dd, J=1.5, 7.5Hz)

48) 5-{4-[2-(4-Methylphenyl)benzoylamino]benzoyl}-1-(4-methyl-1-piperazinylcarbonyl)methyl-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine

NMR ($CDCl_3$, δ) : 1.80-2.18 (2H, m), 2.25-3.56 (4H, m), 2.29 (3H, s), 2.39 (3H, s), 3.00-3.27 (2H, m), 3.41-3.88 (5H, m), 3.98 (1H, d, J=17.5Hz), 4.16 (1H, d, J=17.5Hz), 4.62 (1H, m), 6.52-6.65 (2H, m), 6.82 (1H, d, J=7.5Hz), 6.87-6.96 (3H, m), 7.05-7.55 (10H, m), 7.83 (1H, dd, J=1.5, 7.5Hz)

49) 5-{4-[2-(2,6-Dimethylphenyl)benzoylamino]benzoyl}-1-(4-methyl-1-piperazinylcarbonyl)methyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 1.99 (3H, s), 2.04 (3H, s), 2.36 (3H, s), 2.43-2.68 (5H, m), 2.81 (1H, m), 3.56-3.86 (5H, m), 4.05 (1H, d, J=16Hz), 4.69 (1H, m), 5.18 (1H, d, J=16Hz), 6.69 (1H, d, J=7.5Hz), 6.82-6.96 (3H, m), 7.07 (2H, d, J=8.5Hz), 7.12-7.37 (7H, m), 7.44-7.64 (2H, m), 8.28 (1H, dd, J=1.5, 7.5Hz)

50) 5-{4-[N-2-(4-Methylphenyl)benzoyl-N-methyl]aminobenzoyl}-1-(4-methyl-1-piperazinylcarbonyl)methyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)one

NMR ($CDCl_3$, δ) : 2.35 (3H, s), 2.38 (3H, s), 2.38-2.88 (6H, m), 3.11 (3H, s), 3.47-3.86 (5H, m), 4.02 (1H, d, J=17Hz), 4.67 (1H, m), 5.10 (1H, d, J=17Hz), 5.97 (2H, d, J=8.5Hz), 6.62 (1H, m), 6.69-6.87 (3H, m), 6.94-7.12 (4H, m), 7.21-7.48 (6H, m)

51) 1-{4-[2-(4-Methylphenyl)benzoylamino]benzyl}-5-(4-methyl-1-piperazinylcarbonyl)methyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.26 (3H, s), 2.34 (2H, m), 2.40 (3H, s), 2.53 (2H, t, J=7.5Hz), 3.33 (2H, m), 3.50-3.62 (4H, m), 3.82 (2H, s), 4.87 (2H, m), 6.95-7.23 (9H, m), 7.35-7.56 (7H, m), 7.88 (1H, dd, J=1.5, 7.5Hz)

52) 1-(4-Methyl-1-piperazinylcarbonyl)methyl-5-{4-[2-(2-trifluoromethylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.37 (3H, s), 2.40-2.66 (5H, m), 2.82 (1H, m), 3.58 (2H, m), 3.70 (2H, m), 3.77 (1H, m), 4.05 (1H, d, J=16Hz), 4.70 (1H, m), 5.69 (1H, d, J=16Hz), 6.70 (1H, d, J=7.5Hz), 6.93 (1H, t, J=7.5Hz), 7.00-7.11 (4H, m), 7.15-7.36 (5H, m), 7.43-7.60 (4H, m), 7.73-7.81 (2H, m)

53) 1-(4-Methyl-1-piperazinylcarbonyl)methyl-5-{4-[2-(2,4,6-trimethylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 1.92 (3H, s), 1.99 (3H, s), 2.36 (3H, s), 2.40 (3H, s), 2.42-2.67 (4H, m), 2.83 (1H, m), 3.59 (2H, m), 3.72 (2H, m), 3.80 (1H, m), 4.04 (1H, d, J=17Hz), 4.70 (1H, m), 5.20 (1H, d, J=17Hz), 6.69 (1H, d, J=7.5Hz), 6.75 (2H, d, J=8.5Hz), 6.92 (1H, m), 7.02-7.23 (5H, m), 7.34 (1H, dd, J=1.5, 7.5Hz), 7.44-7.60 (3H, m), 8.25 (1H, dd, J=1.5, 7.5Hz)

54) 5-{2-Methyl-4-[2-(4-methylphenyl)benzoylamino]-benzoyl}-1-(4-methyl-1-piperazinylcarbonyl)methyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

FAB-MASS (m/z) : 630 (M+1)

55) 7-Chloro-1-{4-[2-(4-methylphenyl)benzoylamino]-benzoyl}-5-(4-methyl-1-piperazinylcarbonyl)methyl-2,3,4,5-tetrahydro-1H-1-benzazepine

NMR ($CDCl_3$, δ) : 2.35 (6H, sx2), 2.41 (2H, t, J=5Hz), 2.48 (2H, t, J=5Hz), 3.55-3.72 (4H, m), 1.25-4.50 (7H, m), 6.52 (1H, d, J=7.5Hz), 6.86-7.08 (4H, m), 7.14-7.54 (10H, m), 7.83 (1H, d, J=7.5Hz)

56) 1-{4-[2-(4-Methylphenyl)benzoylamino]benzoyl}-5-(4-methyl-1-piperazinylcarbonyl)methyl-2,3,4,5-tetrahydro-1H-1-benzazepine

FAB-MASS (m/z) : 601 (M+1)

57) 1-{4-[2-(2-Methylphenyl)benzoylamino]benzoyl}-5-(4-methyl-1-piperazinylcarbonyl)methyl-2,3,4,5-tetrahydro-1H-1-benzazepine

FAB-MASS (m/z) : 601 (M+1)

58) 1-{4-[2-(4-Methylphenyl)benzoylamino]benzoyl}-5-(4-methyl-1-piperazinylcarbonyl)methyl-2,3-dihydro-1H-1-benzazepine

FAB-MASS (m/z) : 599 (M+1)

Example 17

[0289] A mixture of 1-(4-aminobenzoyl)-1,2,3,4-tetrahydroquinoline (252 mg), diphenic anhydride (224 mg), triethylamine (202 mg) and catalytic amount of 4-dimethylaminopyridine in dichloromethane (15 ml) was stirred for 8 hours at ambient temperature. The mixture was evaporated in vacuo and diluted with ethyl acetate and washed with saturated sodium hydrogen carbonate aqueous solution, brine, and dried over magnesium sulfate. The solvent was evaporated in vacuo and triturated from ethyl acetate to give 1-{4-[2-(2-carboxyphenyl)benzoylamino]-benzoyl}-1,2,3,4-tetrahyd-

roquinoline (400 mg).

NMR ($CDCl_3$ + CD_3OD, δ) : 1.92-2.13 (2H, m), 2.81 (2H, t, J=7Hz), 3.85 (2H, t, J=7Hz), 6.64 (1H, d, J=9Hz), 6.85 (1H, dd, J=9, 9Hz), 7.00 (1H, dd, J=9, 9Hz), 7.07-7.26 (8H, m), 7.31-7.57 (5H, m), 7.65-7.77 (1H, m), 7.77-7.86 (1H, m)

Example 18

[0290] To a solution of acetyl chloride (1 ml) and methanol (20 ml) was added 1-{4-[2-(2-carboxyphenyl)benzoylamino]-benzoyl}-1,2,3,4-tetrahydroquinoline (350 mg) at 0°C. The solution was stirred for 30 minutes at the same temperature and then stirred for 3 hours at ambient temperature. The solvent was evaporated in vacuo and triturated from dichloromethane to give 1-{4-[2-(2-methoxycarbonylphenyl)benzoylamino]benzoyl}-1,2,3,4-tetrahydroquinoline (300 mg).

NMR ($CDCl_3$, δ) : 1.95-2.11 (2H, m), 2.81 (2H, t, J=7Hz), 3.83 (3H, s), 3.78-3.95 (2H, m), 6.66 (1H, br d, J=9Hz), 6.85 (1H, dd, J=9, 9Hz), 6.99 (1H, dd, J=9, 9Hz), 7.03-7.29 (6H, m), 7.32-7.60 (5H, m), 7.72-7.83 (2H, m), 8.68 (1H, br s)

Example 19

[0291] A solution of 1-{4-[2-(2-methoxycarbonylphenyl)-benzoylamino]benzoyl}-1,2,3,4-tetrahydroquinoline (300 mg) and dry tetrahydrofuran (15 ml) was cooled to 0°C, and lithium aluminum hydride (46 mg) was added. The reaction mixture was maintained at 0°C for 1 hour, and then was quenched by adding 1N hydrochloric acid. The resulting mixture was filtered through a bed of celite, diluted with ethyl acetate, washed with brine, dried over magnesium sulfate, and concentrated. Purification of the residue by column chromatography (silica gel, 15 g; ethyl acetate-n-hexane, 1:2) gave 1-{4-[2-(2-hydroxymethylphenyl)benzoylamino]benzoyl}-1,2,3,4-tetrahydroquinoline (80 mg) as a amorphous.

NMR ($CDCl_3$, δ) : 1.90-2.10 (2H, m), 2.83 (2H, t, J=7Hz), 2.96 (1H, br s), 3.84 (2H, t, J=7Hz), 4.51 (1H, br d, J=11Hz), 4.93 (1H, br d, J=11Hz), 6.66 (1H, d, J=8Hz), 6.85 (1H, dd, J=8, 8Hz), 6.98 (1H, dd, J=8, 8Hz), 7.05-7.86 (13H, m), 8.86 (1H, br s)

Example 20

[0292] To a solution of 1-carboxymethyl-5-{4-[2-(2-methylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (220 mg), 2-dimethylaminoethanol (37 mg) and 4-dimethylaminopyridine (10 mg) in dichloromethane (5 ml) were added dicyclohexylcarbodiimide (102 mg) at ambient temperature and the mixture was stirred at the same temperature for 30 hours. The resulting mixture was washed with saturated sodium bicarbonate aqueous solution. Drying over magnesium sulfate, filtering and the removal of solvents afforded a crude product. The crude product was purified by silica gel column (3% methanol in chloroform). The solvent was evaporated in vacuo and the residue was solidified with diethyl ether to give 1-[(2-dimethylaminoethoxy)-carbonylmethyl]-5-{4-[2-(2-methylphenyl)benzoylamino]-benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (86 mg) as a white powder.

NMR ($CDCl_3$, δ) : 2.08 (3H, s), 2.30 (6H, s), 2.55-2.85 (4H, m), 3.72-3.88 (1H, m), 4.22 (1H, d, J=18Hz), 4.33 (2H, d, J=6Hz), 4.70 (1H, dt, J=5, 14Hz), 4.90 (1H, d, J=18Hz), 6.65-7.62 (15H, m), 8.10 (1H, d, J=9Hz)

Example 21

[0293] The following compound was obtained according to a similar manner to that of Example 20.

[0294] 1-[(2-Dimethylaminoethoxy)carbonylmethyl]-5-{4-[2-(4-methylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 2.32 (6H, s), 2.37 (3H, s), 2.56-2.81 (2H, m), 2.63 (2H, t, J=5Hz), 3.83 (1H, dd, J=5, 11Hz), 4.25 (1H, d, J=18Hz), 4.34 (2H, t, J=5Hz), 4.61-4.80 (1H, m), 4.89 (1H, d, J=18Hz), 6.74 (1H, d, J=8Hz), 6.96 (4H, d, J=9Hz), 7.10 (2H, d, J=8Hz), 7.16-7.36 (5H, m), 7.38-7.59 (3H, m), 7.83 (1H, dd, J=1, 8Hz)

Example 22

[0295] To a solution of 3-chloro-4-[2-(2-methylphenyl)-benzoylamino]benzoic acid (309 mg), diphenyl chlorophosphate (251 mg), 1-ethoxycarbonylmethyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (210 mg) in tetrahydrofuran (15 ml) was added triethylamine (172 mg) at 0°C. The resulting mixture was allowed to warm to ambient temperature where it was maintained for 5 hours. The solvent was evaporated and diluted with ethyl acetate and washed with water, diluted hydrochloric acid, saturated sodium bicarbonate aqueous solution and brine. The organic layer was dried over magnesium sulfate and concentrated to give 5-{3-chloro-4-[2-(2-methylphenyl)-benzoylamino]benzoyl}-1-ethoxycarbonylmethyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (390 mg) which was purified by recrystallization from a mixture of ethyl acetate and n-hexane.

NMR ($CDCl_3$, δ) : 1.31 (3H, t, J=7Hz), 2.12 and 2.14 (total 3H, s), 2.52-2.89 (2H, m), 3.72-3.93 (1H, m), 4.15-4.40 (3H, m), 4.56-4.89 (2H, m), 6.72 (1H, br d, J=8Hz), 6.84-7.09 (2H, m), 7.11-7.40 (8H, m), 7.42-7.76 (3H, m), 7.95 (1H, d, J=8Hz), 8.16-8.35 (1H, m)

Example 23

[0296] The following compounds were obtained according to a similar manner to that of Example 22.

1) 5-{3-chloro-4-[2-(2,4-dimethylphenyl)benzoylamino]-benzoyl}-1-ethoxycarbonylmethyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 1.31 (3H, t, J=7Hz), 2.08 and 2.11 (total 3H, s), 2.33 (3H, s), 2.54-2.90 (2H, m), 3.74-3.92 (1H, m), 4.17-4.40 (3H, m), 4.60-4.86 (1H, m), 4.78 (1H, d, J=17Hz), 6.75 (1H, br d, J=8Hz), 6.85-7.41 (8H, m), 7.41-7.63 (2H, m), 7.72 (1H, br s), 7.90-8.01 (2H, m), 8.22-8.37 (1H, m)

2) 1-Ethoxycarbonylmethyl-5-{4-[2-(2-methylphenyl)-benzoylamino]-3-nitrobenzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 1.30 (3H, t, J=7Hz), 2.17 and 2.18 (total 3H, s), 2.58-2.92 (2H, m), 3.77-3.95 (1H, m), 4.25 (2H, q, J=7Hz), 4.41 (1H, d, J=16Hz), 4.63-4.82 (1H, m), 4.77 (1H, d, J=16Hz), 6.71 (1H, br d, J=8Hz), 6.92-7.73 (11H, m), 7.75-7.93 (2H, m), 8.62 (1H, d, J=8Hz), 10.02 (1H, br s)

3) 1-Ethoxycarbonylmethyl-5-{4-[2-(2,4-dimethylphenyl)-benzoylamino]-2-nitrobenzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 1.35 (3H, t, J=7Hz), 2.01 and 2.03 (total 3H, s), 2.45 (3H, s), 2.55-2.89 (2H, m), 3.73-3.92 (1H, m), 4.18-4.39 (3H, m), 4.84 (1H, d, J=16Hz), 4.82-5.03 (1H, m), 6.84-7.00 (1H, m), 7.03-7.68 (13H, m), 8.08 (1H, d, J=9Hz)

Example 24

[0297] To a solution of 6-[2-(4-methylphenyl)benzoylamino]-nicotinic acid (332 mg) in dichloromethane (5 ml) were added oxalyl chloride (153 mg) and a few drop of N,N-dimethylformamide and the solution was stirred at ambient temperature for 2 hours. Dichloromethane was evaporated in vacuo to give an acid chloride as an oil and the oil was added to a mixture of 1-ethoxycarbonylmethyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (249 mg) and triethylamine (0.167 ml) in dichloromethane (20 ml). The mixture was stirred at ambient temperature for 2 hours and washed successively with 1N hydrochloric acid, water and brine, and dried over magnesium sulfate. The solvent was evaporated in vacuo to give an oil and the oil was subjected to a silica gel column (30 g, 2% methanol in chloroform) to give 1-ethoxycarbonylmethyl-5-{6-[2-(4-methylphenyl)benzoylamino]nicotinoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (250 mg).

NMR ($CDCl_3$, δ) : 1.15-1.33 (3H, m), 2.34 (3H, s), 2.54-2.88 (2H, m), 3.85 (1H, m), 4.17-4.40 (3H, m), 4.65-4.82 (2H, m), 6.74 (1H, d, J=7.5Hz), 7.00 (1H, m), 7.16 (2H, d, J=8.5Hz), 7.20-7.35 (3H, m), 7.38-7.46 (2H, m), 7.48-7.58 (2H, m), 7.70 (1H, m), 7.87 (1H, s), 7.98-8.07 (2H, m)

Example 25

[0298] The following compound was obtained according to a similar manner to that of Example 24.

[0299] 1-Ethoxycarbonylmethyl-5-{2-methoxy-4-[2-(4-methylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one

NMR ($CDCl_3$, δ) : 1.27-1.40 (3H, m), 2.33-2.42 (3H, m), 2.52-2.90 (2H, m), 3.40-3.95 (5H, m), 4.20-4.40 (2H, m), 4.77-5.01 (2H, m), 6.77-7.93 (16H, m)

Example 26

[0300] A mixture of 1-(2-acetoxyethyl)-5-{4-[2-(4-methylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (450 mg) and potassium carbonate (117 mg) in methanol (15 ml) was stirred at ambient temperature for 3 hours. The mixture was diluted with chloroform and the solution was washed with water and brine, and dried over magnesium sulfate. The solvent was evaporated in vacuo to give 1-(2-hydroxyethyl)-5-{4-[2-(4-methylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (430 mg).

NMR ($CDCl_3$, δ) : 2.36 (3H, s), 2.42-2.76 (2H, m), 3.75-4.20 (5H, m), 4.63 (1H, m), 6.93-7.10 (3H, m), 7.07-7.58 (13H, m), 7.81 (1H, d, J=7.5Hz)

Example 27

[0301] To a solution of 1-{4-[2-(2-methylphenyl)benzoylamino]benzoyl}-2,3,4,5-tetrahydro-1H-1-benzazepin-5-one (620 mg) in methanol (20 ml) was added sodium borohydride (49.4 mg) and the mixture was stirred at ambient temperature for 4 hours. The mixture was diluted with chloroform and the solution was washed with water and brine, and dried over magnesium sulfate. The solvent was evaporated in vacuo to give a syrup and the residue was purified by silica gel column (30g, 1% methanol in chloroform) to give 5-hydroxy-1-{4-[2-(2-methylphenyl)-benzoylamino]benzoyl}-2,3,4,5-tetrahydro-1H-1-benzazepine (580 mg).

NMR ($CDCl_3$, δ) : 1.61-1.89 (2H, m), 2.04 (3H, s), 2.21 (1H, m), 2.50 (1H, m), 2.76 (1H, m), 4.73-5.65 (2H, m), 6.56 (1H, d, J=7.5Hz), 6.81 (2H, d, J=8.5Hz), 6.90-7.37 (11H, m), 7.44-7.66 (3H, m), 8.08 (1H, d, J=7.5Hz)

Example 28

[0302] To a solution of oxalyl chloride (0.134 ml) in dichloromethane (10 ml) was added dimethyl sulfoxide (0.109 ml) at -78°C and the mixture was stirred at the same temperature. After 10 minutes, 1-(2-hydroxyethyl)-5-{4-[2-(4-methylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (400 mg) in dichloromethane (10 ml) was added dropwise at -78°C and the mixture was stirred at the same temperature for 30 minutes. To the mixture was added triethylamine (0.537 ml) and the mixture was allowed to ambient temperature. The solution was washed with water and brine, and dried over magnesium sulfate. The solvent was evaporated in vacuo to give 1-formylmethyl-5-{4-[2-(4-methylphenyl)-benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (301 mg) as an unstable oil. The oil was used for next step without further purification.

Example 29

[0303] To a mixture of 1-formylmethyl-5-{4-[2-(4-methylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (380 mg) and 4-methylpiperazine (73.4 mg) in a mixture of methanol (10 ml) and acetic acid (0.5 ml) was added sodium cyanoborohydride (46.1 mg) and the mixture was stirred at ambient temperature for 5 hours. The mixture was poured into a mixture of chloroform and saturated aqueous sodium hydrogen carbonate and the mixture was stirred at ambient temperature for 30 minutes. The solution was extracted with chloroform and washed with brine, and dried over magnesium sulfate. The solvent was evaporated in vacuo and the residue was subjected to a silica gel column (20g, 5% methanol in chloroform). The solvent was evaporated in vacuo and the residue was solidified with diethyl ether to give 5-{4-[2-(4-methylphenyl)benzoylamino]benzoyl}-1-[2-(4-methyl-1-piperazinyl)ethyl]-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (115 mg).

NMR ($CDCl_3$, δ) : 2.30 (3H, s), 2.38 (3H, s), 2.41-2.91 (12H, m), 3.78 (1H, dd, J=6, 12.5Hz), 4.00 (2H, m), 4.67 (1H, dt, J=6, 12.5Hz), 6.72 (1H, br d, J=7.5Hz), 6.90-7.02 (3H, m), 7.10-7.56 (11H, m), 7.83 (1H, dd, J=1.5, 7.5Hz)

Example 30

[0304] To a solution of 1-[(4-tert-butoxycarbonyl-1-piperazinyl)carbonylmethyl]-5-{4-[2-(4-methylphenyl)-benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (150 mg) in ethyl acetate (5 ml) was added 4N hydrogen chloride - ethyl acetate solution, and then the mixture was stirred at ambient temperature for 12 hours. The solvents were evaporated in vacuo and the residue was diluted with saturated aqueous sodium bicarbonate solution, and then the aqueous layer was extracted with ethyl acetate. Drying, filtering and the removal of solvents afforded a crude product. The crude product was chromatographed on silica gel (20% methanol in chloroform) to give 5-{4-[2-(4-methylphenyl)benzoylamino]-benzoyl}-1-[(1-piperazinyl)carbonylmethyl]-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (58 mg) as a white powder.

NMR ($CDCl_3$, δ) : 2.38 (3H, s), 2.63 (1H, dd, J=3, 15Hz), 2.77-3.06 (5H, m), 3.53-3.60 (2H, br), 3.66-3.72 (2H, m), 3.81 (1H, dd, J=7, 14Hz), 4.08 (1H, d, J=15Hz), 4.66-4.78 (1H, m), 5.17 (1H, d, J=15Hz), 6.68-6.75 (1H, br), 6.93-7.01 (3H, m), 7.09 (2H, d, J=8Hz), 7.20 (2H, d, J=9Hz), 7.24-7.32 (3H, m), 7.35-7.43 (3H, m), 7.45-7.57 (2H, m), 7.82 (1H, dd, J=1, 8Hz)

Example 31

[0305] To a solution of 1-{[4-(2-hydroxyethyl)-1-piperazinyl]carbonylmethyl}-5-{4-[2-(4-methylphenyl)-benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (178 mg) and triethylamine (31 mg) in dichloromethane (4 ml) was added acetic anhydride (31 mg) and the mixture was stirred at ambient temperature for 1.5 hours. To the mixture was added 4-dimethylaminopyridine (10 mg) and acetic anhydride (10 mg), and then the mixture was stirred at ambient temperature for 15 minutes. The resulting mixture was diluted with dichloromethane and the organic layer

was washed successively with saturated aqueous sodium bicarbonate solution and brine. Drying, filtering and the removal of solvents afforded a crude product. The crude product was triturated with a mixture of diethyl ether and n-hexane (1:1) to give 1-{[4-(2-acetoxyethyl-1-piperazinyl]-carbonylmethyl}-5-{4-[2-(4-methylphenyl)benzoylamino]-benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (205 mg) as a slightly-yellow powder.

NMR ($CDCl_3$, δ) : 2.09 (3H, s), 2.39 (3H, s), 2.54-2.90 (8H, m), 3.58-3.88 (5H, m), 4.10 (1H, d, J=16Hz), 4.23 (2H, t, J=6Hz), 4.63-4.80 (1H, m), 5.16 (1H, d, J=16Hz), 6.72 (1H, d, J=8Hz), 6.90-7.15 (7H, m), 7.18-7.58 (7H, m), 7.82 (1H, dd, J=1, 8Hz)

Example 32

[0306] A solution of 5-{3-hydroxy-4-[2-(4-methylphenyl)-benzoylamino]benzoyl}-1-[(4-methyl-1-piperazinyl)carbonylmethyl]-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (350 mg), 3-dimethylaminopropyl chloride hydrochloride (96.4 mg) and potassium carbonate (230 mg) in N,N-dimethylformamide (15 ml) were stirred for 4 hours at 80°C. The mixture was diluted with ethyl acetate and washed with water, saturated aqueous sodium bicarbonate and brine. The organic solution was dried over sodium sulfate, concentrated, and purified by silica gel column chromatography (SiO_2 10 g, 15% methanol in chloroform) to give 5-{3-dimethylaminopropoxy-4-[2-(4-methylphenyl)-benzoylamino]benzoyl}-1-[(4-methyl-1-piperazinyl)-carbonylmethyl]-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (150 mg).

NMR ($CDCl_3$, δ) : 1.74 (2H, s), 2.15 (6H, s), 2.32 (3H, s), 2.33 (3H, s), 2.08-2.67 (7H, m), 2.82 (1H, m), 3.46-3.92 (7H, m), 4.06 (1H, d, J=15Hz), 4.69 (1H, m), 5.18 (1H, d, J=15Hz), 6.43 (1H, br d, J=9Hz), 6.72 (1H, br d, J=9Hz), 6.96 (1H, dd, J=9, 9Hz), 7.00-7.56 (10H, m), 7.68 (1H, d, J=9Hz), 7.86 (1H, s), 8.16 (1H, d, J=9Hz)

Example 33

[0307] To a solution of 1-ethoxycarbonylmethyl-5-{4-[2-(4-methylphenyl)benzoylamino]benzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (377 mg) in N,N-dimethylformamide (5 ml) was added sodium hydride (60% in oil, 19.3 mg) and the mixture was stirred at ambient temperature for 30 minutes. Methyl iodide (143 mg) was added to the solution and the mixture was stirred at ambient temperature for 8 hours. The mixture was diluted with ethyl acetate and washed successively with 1N hydrochloric acid, aqueous sodium hydrogen carbonate and brine, and dried over magnesium sulfate. The solvent was evaporated in vacuo and the residue was purified by silica gel column (20g, 1% methanol in chloroform) to give 1-ethoxycarbonylmethyl-5-{4-[N-2-(4-methylphenyl)benzoyl-N-methyl]aminobenzoyl}-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (390 mg).

NMR ($CDCl_3$, δ) : 1.33 (3H, t, J=7.5Hz), 2.39 (3H, s), 2.52-2.82 (2H, m), 3.10 (3H, s), 3.77 (1H, m), 4.08-4.34 (3H, m), 4.66 (1H, m), 4.78 (1H, d, J=17Hz), 5.99 (2H, d, J=8.5Hz), 6.61-6.84 (4H, m), 6.93-7.10 (4H, m), 7.21-7.33 (5H, m), 7.47 (1H, m)

Example 34

[0308] A solution of 5-{4-[2-(4-methylphenyl)benzoylamino]-benzoyl}-1-[(4-methyl-1-piperazinyl) carbonylmethyl]-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (130 mg), di-tert-butyldicarbonate (150 mg), triethylamine (64 mg) and 4-dimethylaminopyridine (catalytic amount) in acetone (10 ml) was stirred for 5 hours at ambient temperature. The solvent was washed with water, saturated sodium bicarbonate aqueous solution and brine, and dried over sodium sulfate. The solvent was evaporated and purified by silica gel column chromatography (30 g, 5% methanol in chloroform) to give 5-{4-[N-tert-butoxycaxbonyl-2-(4-methylphenyl)benzoylamino]benzoyl}-1-[(4-methyl-1-piperazinyl)carbonylmethyl]-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (120 mg).

NMR ($CDCl_3$, δ) : 1.12 (9H, s), 2.34 (3H, s), 2.41 (3H, s), 2.38-2.69 (5H, m), 2.76-2.94 (1H, m), 3.51-3.71 (3H, m), 3.72-3.90 (2H, m), 4.07 (1H, d, J=15Hz), 4.64-4.83 (1H, m), 5.14 (1H, d, J=15Hz), 6.60-6.80 (3H, m), 6.88-7.01 (1H, m), 7.12-7.53 (12H, m)

Example 35

[0309] A mixture of 5-{4-[2-(4-methylphenyl)benzoylamino]-benzoyl}-1-(4-methyl-1-piperazinylcarbonyl)methyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (110 mg) and methyl iodide (76.1 mg) in dichloromethane (10 ml) was stirred at ambient temperature overnight and a precipitate was filtered to give 4-{5-{4-[2-(4-methylphenyl)benzoylamino]-benzoyl}-2-oxo-1,3,4,5-tetrahydro-2H-1,5-benzodiazepin-1-yl)acetyl-1,1-dimethylpiperazinium iodide (118 mg).

NMR (DMSO-d_6, δ) : 2.29 (3H, s), 2.44-2.71 (2H, m), 3.19 (6H, s), 3.38-3.56 (4H, m), 3.72 (1H, m), 3.87-4.02 (4H, m), 4.41 (1H, m), 4.48 (1H, d, J=17.5Hz), 5.60 (1H, d, J=17.5Hz), 6.84 (1H, d, J=7.5Hz), 7.02 (1H, m), 7.08-7.17 (4H, m), 7.25-7.31 (4H, m), 7.37-7.56 (7H, m)

Example 36

[0310] To a solution of 5-{4-[2-(4-methylphenyl)-benzoylamino]benzoyl}-1-(4-methyl-1-piperazinylcarbonyl)-methyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (12.2 g) in hot ethanol (125 ml) was added sulfuric acid (972 mg) in ethanol (10 ml) and the solution was gently stirred at 80°C for 1 hour. The solution was cooled to ambient temperature and the precipitated solid was filtered and dired in air to give 5-{4-[2-(4-methylphenyl)benzoylamino]benzoyl}-1-(4-methyl-1-piperazinylcarbonyl)methyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one 1/2sulfate (12.1 g).

NMR (DMSO-d_6, δ) : 2.28 (3H, s), 2.43-3.81 (11H, m), 2.59 (3H, s), 4.45 (1H, m), 4.52 (1H, d, J=17.5Hz), 5.07 (1H, d, J=17.5Hz), 6.82 (1H, d, J=7.5Hz), 7.01 (1H, m), 7.07-7.60 (15H, m)

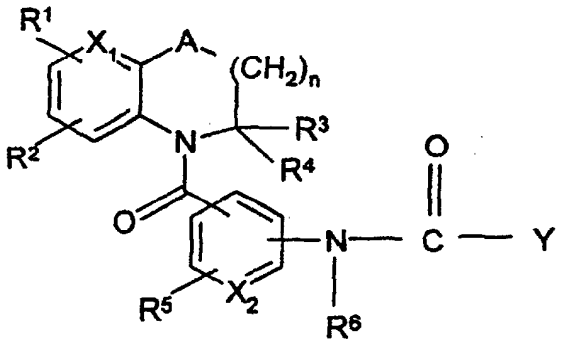
Example 37

[0311] To a solution of 5-{4-[2-(4-methylphenyl)benzoylamino]benzoyl}-1-(4-methyl-1-piperazinylcarbonyl)methyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one (12.2 g) in hot ethanol (125 ml) was added methanesulfonic acid (1.90 g) in ethanol (10 ml). The solution was cooled to ambient temperature and the precipitated solid was filtered and dried in air to give 5-{4-[2-(4-methylphenyl)-benzoylamino]benzoyl}-1-(4-methyl-1-piperazinylcarbonyl)-methyl-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one methanesulfonate (13.7 g).

NMR (DMSO-d_6, δ) : 2.26 (3H, s), 2.32 (3H, s), 2.43-3.60 (10H, m), 2.73 (3H, s), 3.71 (1H, m), 4.36-4.57 (2H, m), 5.10 (1H, d, J=17.5Hz), 6.80 (1H, d, J=7.5Hz), 7.00 (1H, m), 7.09-7.58 (15H, m), 9.80 (1H, br)

Claims

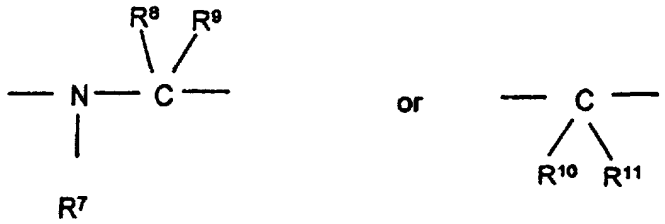
1. A compound of the formula:



(I)

wherein

- R^1 is hydrogen or (C_1-C_6) alkyl,
- R^2 is hydrogen, (C_1-C_6) alkyl, halo (C_1-C_6) alkyl, halogen or (C_1-C_6) alkoxy,
- R^3 and R^4 are each hydrogen, (C_1-C_6) alkyl or taken together to form oxo,
- R^5 is hydrogen, halogen, nitro, hydroxy, (C_1-C_6)alkoxy(C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkoxy(C_1-C_6) alkoxy, phenyl(C_1-C_6)alkoxy, nitrophenyl(C_1-C_6)alkoxy, (C_1-C_6)alkanoyloxy, benzoyloxy, fluorenecarbonyloxy, (C_1-C_6)alkoxycarbonyloxy, phenyl(C_1-C_6)alkoxycarbonyloxy, halophenyl(C_1-C_6)alkoxycarbonyloxy, tri(C_1-C_6)alkylsilyloxy, (C_1-C_6) alkyl or (C_1-C_6) alkoxy optionally substituted with (C_1-C_6) alkylamino,
- R^6 is hydrogen, (C_1-C_6) alkyl or (C_1-C_6) alkoxycarbonyl,
- A is



in which

R^7 is hydrogen; (C_1-C_6) alkyl optionally substituted with halogen, amino, (C_1-C_6) alkylamino, (C_1-C_6) alkanoylamino, halo(C_1-C_6)alkanoylamino, phthaloylamino, (C_1-C_6)alkoxycarbonylamino, benzyloxycarbonylamino, nitrobenzyloxycarbonylamino, benzenesulfonylamino, tosylamino, nitrophenylsulfenylamino, tritylamino, benzylamino, carboxy, (C_1-C_6)alkoxycarbonyl, di(C_1-C_6)alkylamino (C_1-C_6)alkoxycarbonyl, halo(C_1-C_6)alkoxycarbonyl, trihalo(C_1-C_6)alkoxycarbonyl, phenoxycarbonyl, nitrophenoxycarbonyl, naphthyloxycarbonyl, phenyl(C_1-C_6)alkoxycarbonyl, nitrophenyl(C_1-C_6) alkoxycarbonyl, carbamoyl, (C_1-C_6) alkylcarbamoyl, trihalo(C_1-C_6)alkanoyl, unsubstituted (C_1-C_6) alkanoyl, toluoyl, di(tert-butyl)benzoyl, tolylbenzoyl, aminobenzoyl, tolylbenzoylaminobenzoyl, unsubstituted benzoyl, an N-containing heterocyclic carbonyl, (C_1-C_6) alkylsulfonyl, tolylsulfonyl, di (C_1-C_6)alkoxyphenylsulfonyl, unsubstituted phenylsulfonyl, piperidyl, pyridyl, N-(C_1-C_6) alkylpiperazinyl, hydroxy, (C_1-C_6)alkoxy(C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C_1-C_6)alkoxy(C_1-C_6)alkoxyl phenyl (C_1-C_6)alkoxy, nitrophenyl(C_1-C_6)alkoxy, (C_1-C_6)alkanoyloxy, benzoyloxy, fluorenecarbonyloxy, (C_1-C_6)alkoxycarbonyloxy, phenyl(C_1-C_6)alkoxycarbonyloxy, halophenyl(C_1-C_6)alkoxycarbonyloxy, tri(C_1-C_6)alkylsilyloxy or dimethoxyphenylsulfonyl; and

R^8 and R^9 are taken together to form oxo or thioxo;

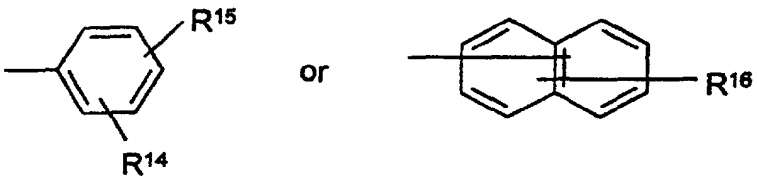
R^{10} is hydrogen;

R^{11} is hydrogen, or (C_1-C_6) alkylamino;

X_1 is CH,

X_2 is CH or N,

Y is



in which

R^{14} is hydrogen, halogen, hydroxy or (C_1-C_6) alkoxy,

R^{15} is phenoxy, naphthyl, phenyl substituted with substituent(s) selected from the group consisting of (C_1-C_6) alkyl, (C_1-C_6) alkoxy, halogen, halo (C_1-C_6) alkyl, hydroxy, amino (C_1-C_6) alkyl, azido (C_1-C_6) alkyl, (C_1-C_6) alkylamino (C_1-C_6) alkyl, (C_1-C_6) alkanoylamino (C_1-C_6) alkyl, hydroxy (C_1-C_6) alkyl, cyano, carboxy, (C_1-C_6)alkoxycarbonyl, di(C_1-C_6)alkylamino(C_1-C_6)alkoxycarbonyl, halo(C_1-C_6)alkoxycarbonyl, trihalo (C_1-C_6)alkoxycarbonyl, phenoxycarbonyl, nitrophenoxycarbonyl, naphthyloxycarbonyl, phenyl(C_1-C_6) alkoxycarbonyl, nitrophenyl(C_1-C_6)alkoxycarbonyl, pyridyl or pyrrolyl, and

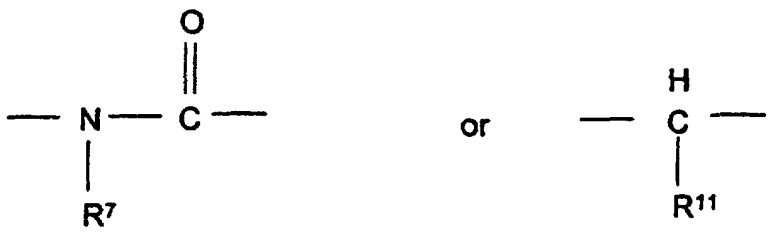
R^{16} is tolyl and

n is 0, 1, 2 or 3,

and pharmaceutically acceptable salts thereof.

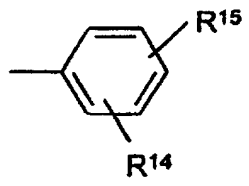
2. A compound according to claim 1, wherein

R^1 is hydrogen,
R^2 is hydrogen, (C_1-C_6) alkyl or halogen,
R^3 is hydrogen,
R^4 is hydrogen,
R^5 is hydrogen or (C_1-C_6) alkoxy,
R^6 is hydrogen,
A is



in which

R^7 is hydrogen; or (C_1-C_6) alkyl optionally substituted with amino, (C_1-C_6) alkylamino, (C_1-C_6)alkanoylamino, halo(C_1-C_6)alkanoylamino, phthaloylamino, (C_1-C_6)alkoxycarbonylamino, benzyloxycarbonylamino, nitrobenzyloxycarbonylamino, benzenesulfonylamino, tosylamino, nitrophenylsulfenylamino, tritylamino, benzylamino, carboxy, (C_1-C_6)alkoxycarbonyl, di(C_1-C_6)alkylamino(C_1-C_6)alkoxycarbonyl, halo(C_1-C_6) alkoxycarbonyl, trihalo(C_1-C_6)alkoxycarbonyl, phenoxycarbonyl, nitrophenoxycarbonyl, naphthyloxycarbonyl, phenyl(C_1-C_6)alkoxycarbonyl, nitrophenyl(C_1-C_6)alkoxycarbonyl, carbamoyt, (C_1-C_6)alkylcarbamoyl, trihalo(C_1-C_6)alkanoyl, unsubstituted (C_1-C_6)alkanoyl, toluoyl, di(tert-butyl)benzoyl, tolylbenzoyl, aminobenzoyl, tolylbenzoylaminobenzoyl, unsubstituted benzoyl, an N-containing heterocyclic carbonyl, (C_1-C_6)alkylsulfonyl, tolylsulfonyl, di(C_1-C_6)alkoxyphenylsuffonyl, unsubstituted phenylsulfonyl, piperidyl, pyridyl, N-(C_1-C_6) alkylpiperazinyl; and
R^{11} is hydrogen or (C_1-C_6)alkylamino,
X_1 is CH,
X_2 is CH,
Y is

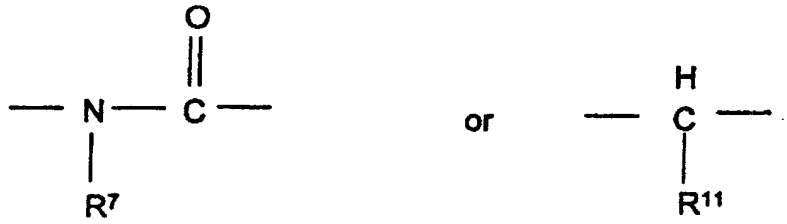


in which

R^{14} and R^{15} are each as defined above, and
n is 0, 1 or 2.

3. A compound according to claim 2, wherein

A is

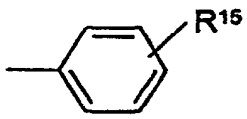


in which

R^7 is lower alkyl optionally substituted with amino, (C_1-C_6) alkylamino, (C_1-C_6)alkanoylamino, halo(C_1-C_6)alkanoylamino, phthaloylamino, (C_1-C_6)alkoxycarbonylamino, benzyloxycarbonylamino, nitrobenzyloxycarbonylamino, benzenesulfonylamino, tosylamino, nitrophenytsulfenylamino, tritylamino, benzylamino, carboxy, (C_1-C_6)alkoxycarbonyl, di(C_1-C_6)alkylamino(C_1-C_6)alkoxycarbonyl, halo(C_1-C_6)alkoxycarbonyl, trihalo(C_1-C_6)alkoxycarbonyl, phenoxycarbonyl, nitrophenoxycarbonyl, naphthyloxycarbonyl, phenyl(C_1-C_6) alkoxycarbonyl, nitrophenyl(C_1-C_6)alkoxycarbonyl, carbamoyl, (C_1-C_6) alkylcarbamoyl, trihalo(C_1-C_6)alkanoyl, unsubstituted (C_1-C_6) alkanoyl, toluoyl, di(tert-butyl)benzoyl, tolylbenzoyl, aminobenzoyl, tolylbenzoylaminobenzoyl, unsubstituted benzoyl, an N-containing heterocyclic carbonyl, (C_1-C_6) alkylsulfonyl, tolylsulfonyl, di(C_1-C_6)alkoxyphenylsulfonyl, unsubstituted phenylsulfonyl or piperidino; and

R^{11} is hydrogen or (C_1-C_6) alkylamino, and

Y is

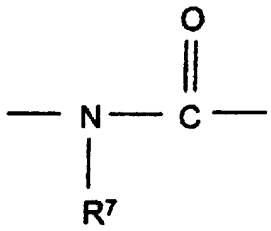


in which

R^{15} is phenyl substituted with substituent(s) selected from the group consisting (C_1-C_6) alkyl, (C_1-C_6) alkoxy, halogen, halo (C_1-C_6)alkyl, hydroxy, amino (C_1-C_6)alkyl, azido (C_1-C_6)alkyl, (C_1-C_6) alkylamino (C_1-C_6) alkyl, (C_1-C_6)alkanoylamino(C_1-C_6) alkyl, hydroxy(C_1-C_6) alkyl, cyano, carboxy, (C_1-C_6)alkoxycarbonyl, di (C_1-C_6)alkylamino(C_1-C_6)alkoxycarbonyl, halo(C_1-C_6)alkoxycarbonyl, trihalo(C_1-C_6)alkoxycarbonyl, phenoxycarbonyl, nitrophenoxycarbonyl, naphthyloxycarbonyl, phenyl(C_1-C_6)alkoxycarbonyl and nitrophenyl (C_1-C_6)alkoxycarbonyl.

4. A compound according to claim 3,

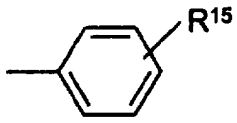
A is



in which

R^7 is (C_1-C_6) alkyl substituted with N-(C_1-C_6) alkylpiperazinylcarbonyl or(C_1-C_6) alkyl substituted with di (C_1-C_6) alkylamino, and

Y is

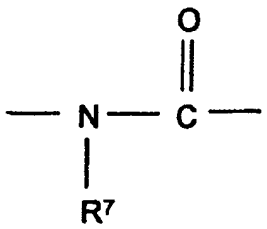


in which

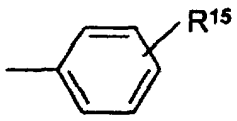
R^{15} is phenyl substituted with (C_1-C_6) alkyl or di (C_1-C_6) alkyl.

5. A compound according to claim 4, wherein

R^2 is hydrogen,
R^5 is hydrogen,
A is



R^7 is (C_1-C_6) alkyl substituted with N-(C_1-C_6) alkylpiperazinylcarbonyl
Y is

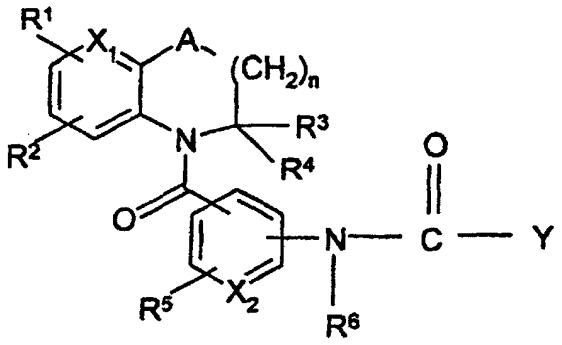


in which

R^{15} is phenyl substituted with (C_1-C_6) alkyl or di (C_1-C_6) alkyl and
n is 1.

6. A compound of claim 5, which is 5-{4-[2-(4-methylphenyl)benzoylamino]benzoyl}-1-[(4-methyl-1-piperazinyl)carbonylmethyl]-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-one.

7. A process for preparing a compound of the formula



(I)

wherein

R^1 is hydrogen or $(C_1\text{-}C_6)$ alkyl,

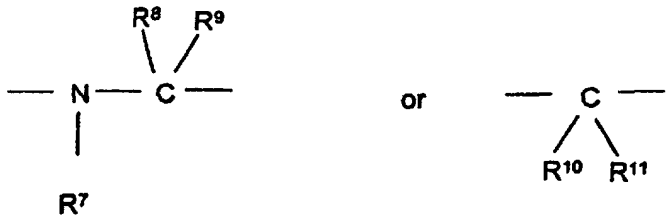
R^2 is hydrogen, $(C_1\text{-}C_6)$ alkyl, halo $(C_1\text{-}C_6)$ alkyl, halogen or $(C_1\text{-}C_6)$ alkoxy,

R^3 and R^4 are each hydrogen, $(C_1\text{-}C_6)$ alkyl or taken together to form oxo,

R^5 is hydrogen, halogen, nitro, hydroxy, $(C_1\text{-}C_6)$alkoxy$(C_1\text{-}C_6)$alkoxy, $(C_1\text{-}C_6)$alkoxy$(C_1\text{-}C_6)$alkoxy $(C_1\text{-}C_6)$alkoxy, phenyl$(C_1\text{-}C_6)$alkoxy, nitrophenyl$(C_1\text{-}C_6)$alkoxy, $(C_1\text{-}C_6)$alkanoyloxy, benzoyloxy, fluorenecarbonyloxy, $(C_1\text{-}C_6)$alkoxycarbonyloxy, phenyl$(C_1\text{-}C_6)$alkoxycarbonyloxy, halophenyl$(C_1\text{-}C_6)$ alkoxycarbonyloxy, tri$(C_1\text{-}C_6)$alkylsilyloxy, $(C_1\text{-}C_6)$ alkyl or $(C_1\text{-}C_6)$ alkoxy optionally substituted with $(C_1\text{-}C_6)$ alkylamino,

R^6 is hydrogen, $(C_1\text{-}C_6)$ alkyl or $(C_1\text{-}C_6)$ alkoxycarbonyl,

A is



in which

R^7 is hydrogen; $(C_1\text{-}C_6)$ alkyl optionally substituted with halogen, amino, $(C_1\text{-}C_6)$ alkylamino, $(C_1\text{-}C_6)$ alkanoylamino, halo$(C_1\text{-}C_6)$alkanoylamino, phthaloylamino, $(C_1\text{-}C_6)$alkoxycarbonylamino, benzyloxycarbonylamino, nitrobenzyloxycarbonylamino, benzenesulfonylamino, tosylamino, nitrophenylsulfenylamino, tritylamino, benzylamino, carboxy, $(C_1\text{-}C_6)$alkoxycarbonyl, di$(C_1\text{-}C_6)$alkylamino $(C_1\text{-}C_6)$alkoxycarbonyl, halo$(C_1\text{-}C_6)$alkoxycarbonyl, trihalo$(C_1\text{-}C_6)$alkoxycarbonyl, phenoxycarbonyl, nitrophenoxycarbonyl, naphthyloxycarbonyl, phenyl$(C_1\text{-}C_6)$alkoxycarbonyl, nitrophenyl$(C_1\text{-}C_6)$ alkoxycarbonyl, carbamoyl, $(C_1\text{-}C_6)$ alkyl carbamoyl, trihalo$(C_1\text{-}C_6)$alkanoyl, unsubstituted $(C_1\text{-}C_6)$ alkanoyl, toluoyl, di(tert-butyl)benzoyl, tolylbenzoyl, aminobenzoyl, tolylbenzoylaminobenzoyl, unsubstituted benzoyl, an N-containing heterocyclic carbonyl, $(C_1\text{-}C_6)$ alkylsulfonyl, tolylsulfonyl, di $(C_1\text{-}C_6)$alkoxyphenylsulfonyl, unsubstituted phenylsulfonyl, piperidyl, pyridyl, N-$(C_1\text{-}C_6)$ alkylpiperazinyl, hydroxy, $(C_1\text{-}C_6)$alkoxy$(C_1\text{-}C_6)$alkoxy, $(C_1\text{-}C_6)$alkoxy$(C_1\text{-}C_6)$alkoxy$(C_1\text{-}C_6)$alkoxy, phenyl $(C_1\text{-}C_6)$alkoxy, nitrophenyl$(C_1\text{-}C_6)$alkoxy, $(C_1\text{-}C_6)$alkanoyloxy, benzoyloxy, fluorenecarbonyloxy, $(C_1\text{-}C_6)$alkoxycarbonyloxy, phenyl$(C_1\text{-}C_6)$alkoxycarbonyloxy, halophenyl$(C_1\text{-}C_6)$alkoxycarbonyloxy, tri$(C_1\text{-}C_6)$alkylsilyloxy or dimethoxyphenylsulfonyl; and

R^8 and R^9 are taken together to form oxo or thioxo; or

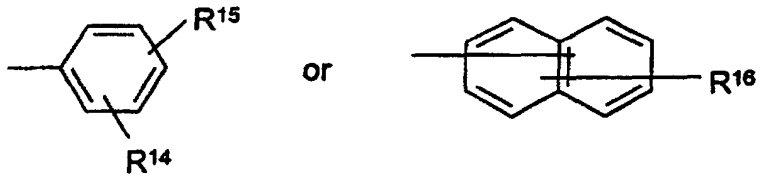
R^{10} is hydrogen;

R^{11} is hydrogen, or $(C_1\text{-}C_6)$ alkylamino;

X_1 is CH,

X_2 is CH or N,

Y is



in which

R^{14} is hydrogen, halogen, hydroxy or (C_1-C_6) alkoxy,

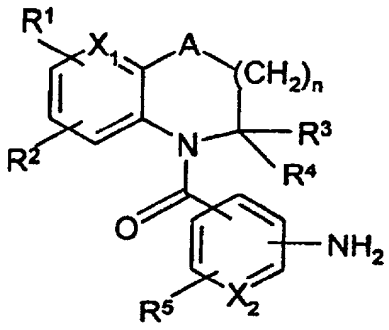
R^{15} is phenoxy, naphthyl, phenyl substituted with substituent(s) selected from the group consisting of (C_1-C_6) alkyl, (C_1-C_6) alkoxy, halogen, halo (C_1-C_6) alkyl, hydroxy, amino (C_1-C_6) alkyl, azido (C_1-C_6) alkyl, (C_1-C_6) alkylamino (C_1-C_6) alkyl, (C_1-C_6) alkanoylamino (C_1-C_6) alkyl, hydroxy (C_1-C_6) alkyl, cyano, carboxy, (C_1-C_6)alkoxycarbonyl, di(C_1-C_6)alkylamino(C_1-C_6)alkoxycarbonyl, halo(C_1-C_6)alkoxycarbonyl, trihalo (C_1-C_6)alkoxycarbonyl, phenoxycarbonyl, nitrophenoxycarbonyl, naphthyloxycarbonyl, phenyl(C_1-C_6) alkoxycarbonyl, nitrophenyl(C_1-C_6)alkoxycarbonyl, pyridyl or pyrrolyl, and

R^{16} is tolyl and

n is 0, 1, 2 or 3,

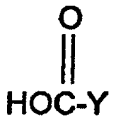
or salts thereof, which comprises,

a) reacting a compound of the formula:



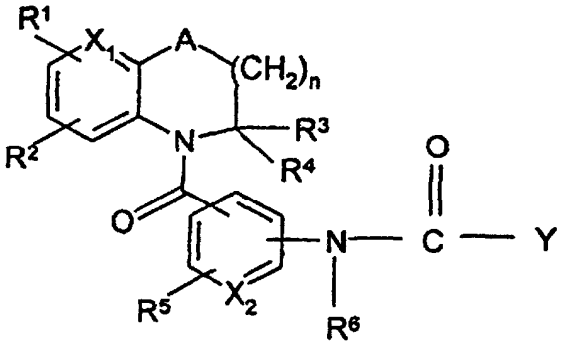
(II)

or its salt with a compound of the formula :



(III)

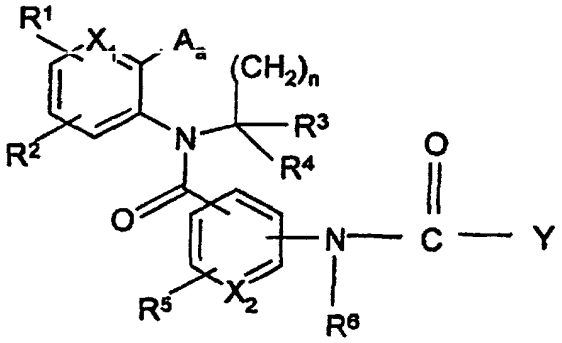
or its reactive derivative at the carboxy group or a salt thereof to provide a compound of the formula :



(Ia)

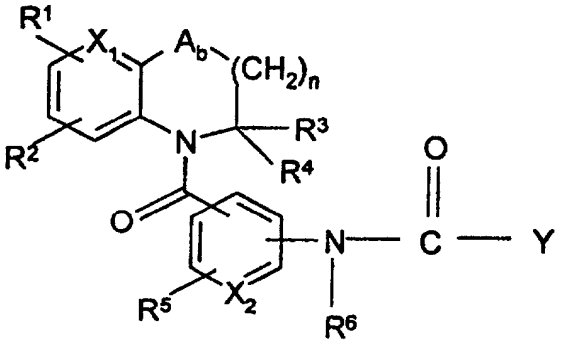
or its salt, in the above formulas, R^1, R^2, R^3, R^4, R^5, A, X_1, X_2, Y and n are each as defined above, or

b) reacting a compound of the formula :



(Ib)

or its reactive derivative at the carboxy group or a salt thereof with an amine to provide a compound of the formula:

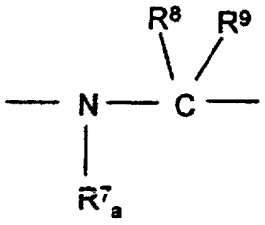


(Ic)

or its salt, in the above formulas,

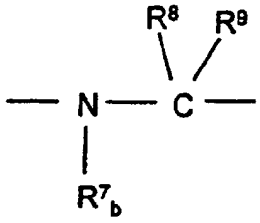
R^1, R^2, R^3, R^4, R^5, R^6, X_1, X_2, Y and n are each as defined above,

A_a is



in which

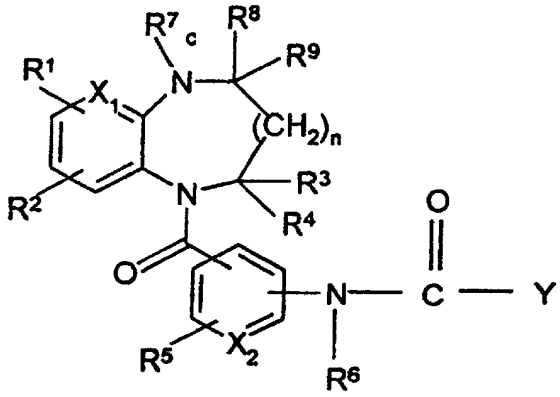
R^8 and R^9 are each as defined above;
$R^7{}_a$ is (C_1-C_6)alkyl substituted with carboxy, and
A_b is



in which

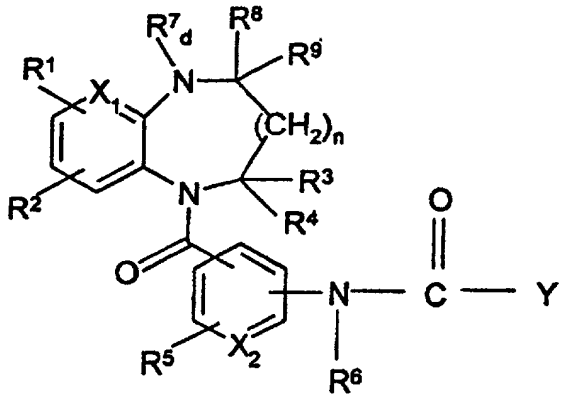
R^8 and R^9 are each as defined above;
$R^7{}_b$ is (C_1-C_6)alkyl substituted with carbamoyl which may be substituted with (C_1-C_6)alkyl, or an N-containing heterocyclic carbonyl; or

c) subjecting a compound of the formula



(Id)

or its salt to elimination reaction of the
N-protective group to provide a compound of the formula :



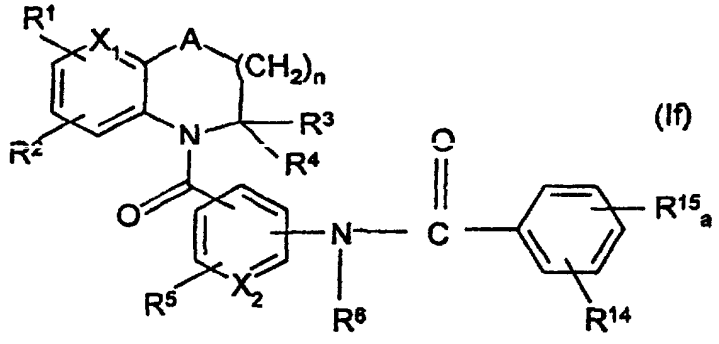
(Ie)

or its salt, in the above formulas,

R^1, R^2, R^3, R^4, R^5, R^6, R^8, R^9, X_1, X_2, Y and n	are each as defined above,
$R^7{}_c$	is (C_1-C_6) alkyl substituted with (C_1-C_6)alkanoylamino, halo (C_1-C_6)alkanoylamino, phthaloylamino, (C_1-C_6)alkoxycarbonylamino, benzyloxycarbonylamino, nitrobenzyloxycarbonylamino, benzenesulfonylamino, tosylamino, nitrophenylsulfenylamino, tritylamino, benzylamino or N-(C_1-C_6) alkoxycarbonylpiperazinylcarbonyl, and
$R^7{}_d$	is (C_1-C_6) alkyl substituted with amino or piperazinylcarbonyl,

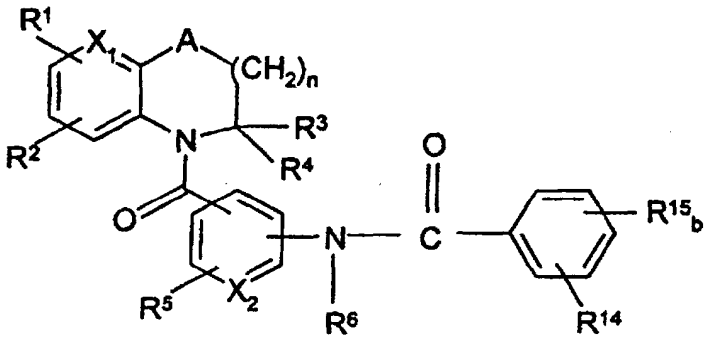
or

d) subjecting a compound of the formula :



(If)

or its salt to reduction to provide a compound of the formula:

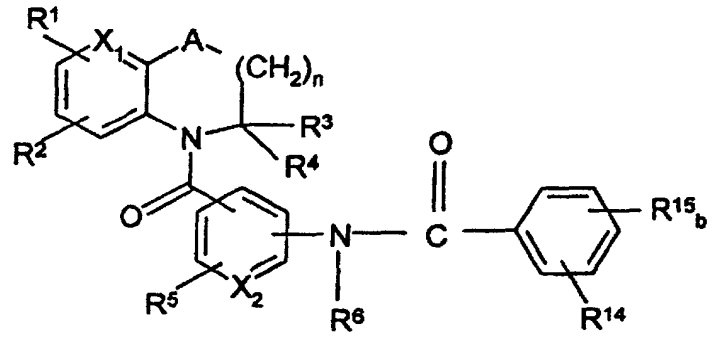


(Ig)

or its salt, in the above formulas,

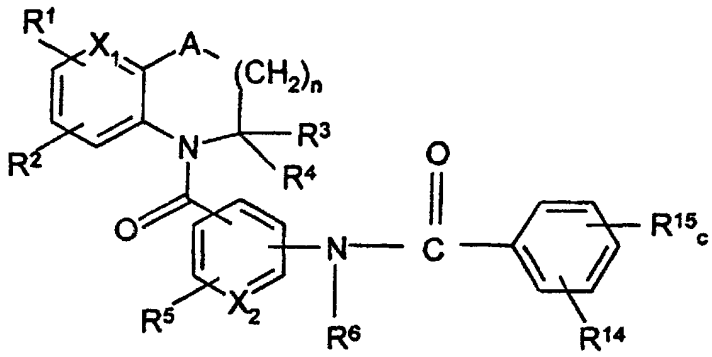
R^1, R^2, R^3, R^4, R^5, R^6, R^{14}, A, X_1, X_2 and n	are each as defined above,
$R^{15}{}_a$	is phenyl substituted with azido (C_1-C_6)alkyl, and
$R^{15}{}_b$	is phenyl substituted with amino(C_1-C_6) alkyl, or

e) reacting a compound of the formula :



(Ig)

or its salt with an acylating agent to provide a compound of the formula:



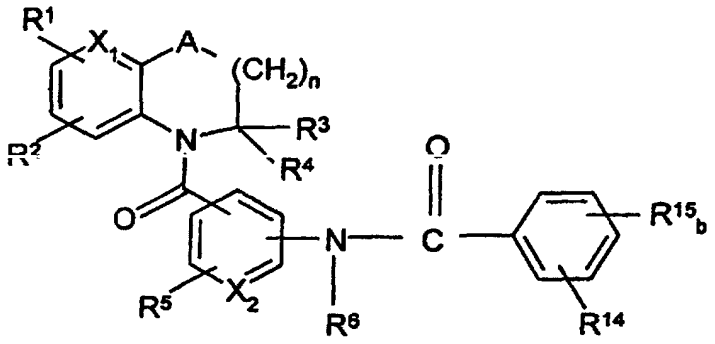
(Ih)

or its salt, in the above formulas,

R^1, R^2, R^3, R^4, R^5, R^6, R^{14}, $R^{15}{}_b$, A, X_1, X_2 and n	are each as defined above, and
$R^{15}{}_c$	is phenyl substituted with (C_1-C_6)alkanoylamino(C_1-C_6)

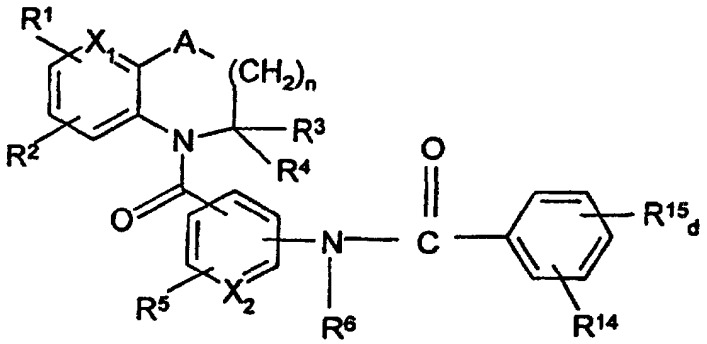
alkyl,

f) reacting a compound of the formula :



(Ig)

or its salt with an alkylating agent to provide a compound of the formula:



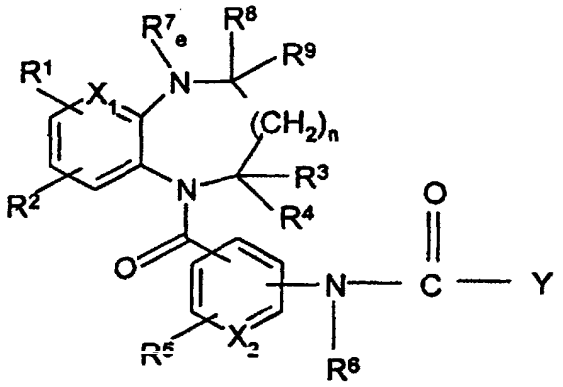
(Ii)

or its salt, in the above formulas,

R^1, R^2, R^3, R^4, R^5, R^6, R^{14}, $R^{15}{}_b$, A, X_1, X_2 and n are each as defined above, and

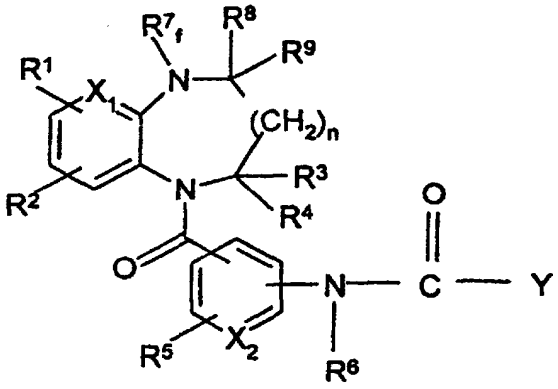
$R^{15}{}_d$ is phenyl substituted with $(C_1\text{-}C_6)$alkylamino$(C_1\text{-}C_6)$ alkyl, or

g) reacting a compound of the formula :



(Ij)

or its salt with an alkylating agent to provide a compound of the formula:

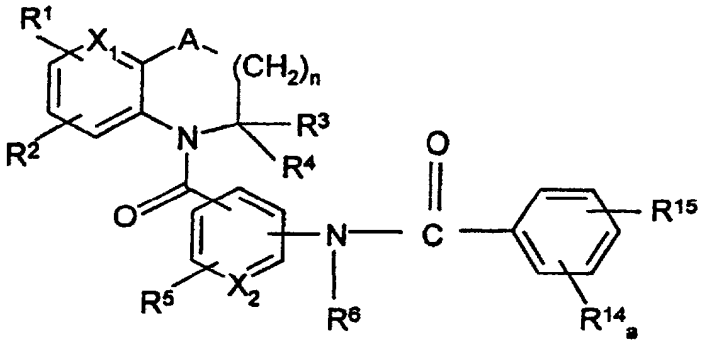


(Ik)

or its salt, in the above formulas,

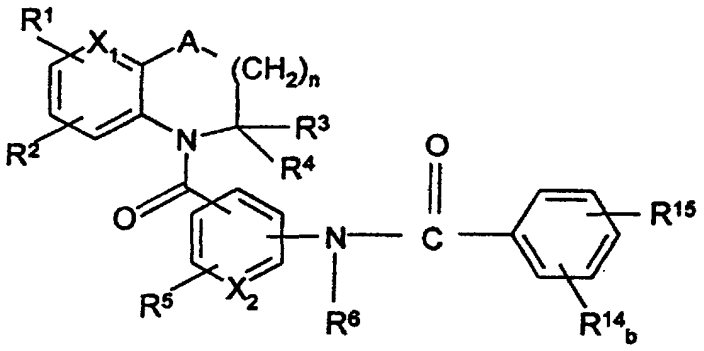
R^1, R^2, R^3, R^4, R^5, R^6, R^8, R^9, X_1, X_2, Y and n	are each as defined above,
$R^7{}_e$	is (C_1-C_6)alkyl substituted with amino, and
$R^7{}_f$	is (C_1-C_6)alkyl substituted with (C_1-C_6)alkylamino, or

h) subjecting a compound of the formula :



(Il)

or its salt to dealkylation reaction to provide a compound of the formula:

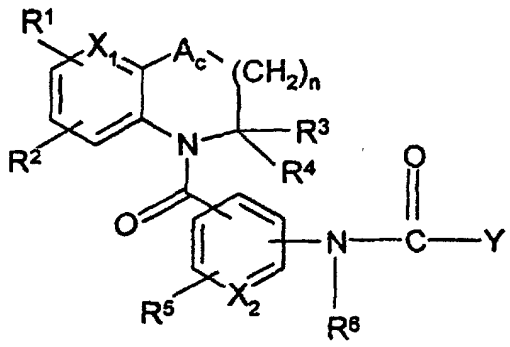


(Im)

or its salt, in the above formulas,

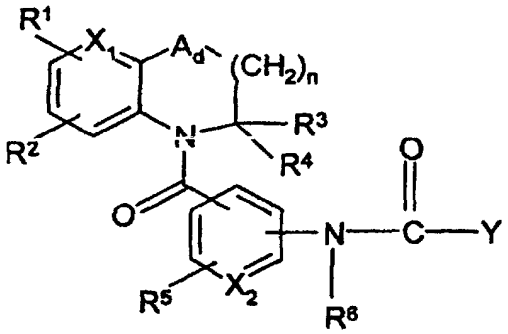
R^1, R^2, R^3, R^4, $R^{5'}$, R^6, R^{15}, A, X_1, X_2 and n	are each as defined above,
$R^{14}{}_a$	is (C_1-C_6)alkoxy, and
$R^{14}{}_b$	is hydroxy, or

i) subjecting a compound of the formula:



(In)

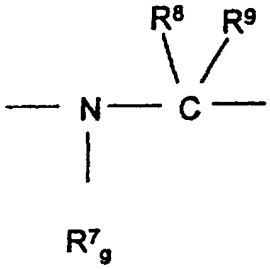
or its salt to deesterification reaction to provide a compound of the formula:



(Io)

or its salt, in the above formulas,

R^1, R^2, R^3, R^4, R^5, R^6, X_1, X_2, Y and n	are each as defined above,
A_c	is

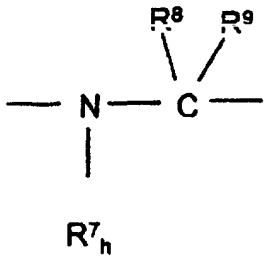


in which

R^8 and R^9	are each as defined above;

$R^7{}_g$ is (C_1-C_6)alkyl substituted with (C_1-C_6)alkoxycarbonyl, di(C_1-C_6)alkylamino(C_1-C_6)alkoxycarbonyl, halo(C_1-C_6)alkoxycarbonyl, trihalo(C_1-C_6)alkoxycarbonyl, phenoxycarbonyl, nitrophenoxycarbonyl, naphthyloxycarbonyl, phenyl(C_1-C_6)alkoxycarbonyf, nitrophenyl(C_1-C_6)alkoxycarbonyl or N-[(C_1-C_6)alkoxycarbonyl(C_1-C_6)alkyl]piperazinylcarbonyl; and

A_d is

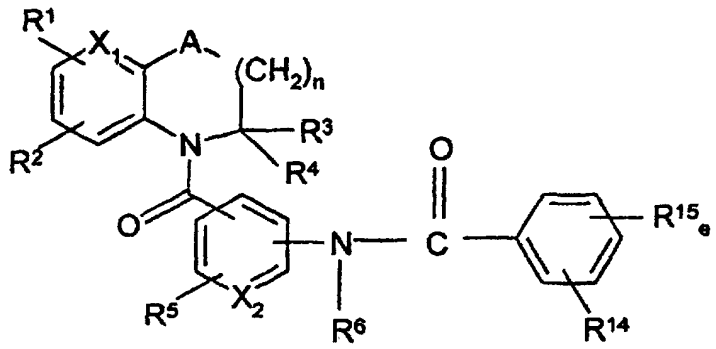


in which

R^8 and R^9 are each as defined above, and

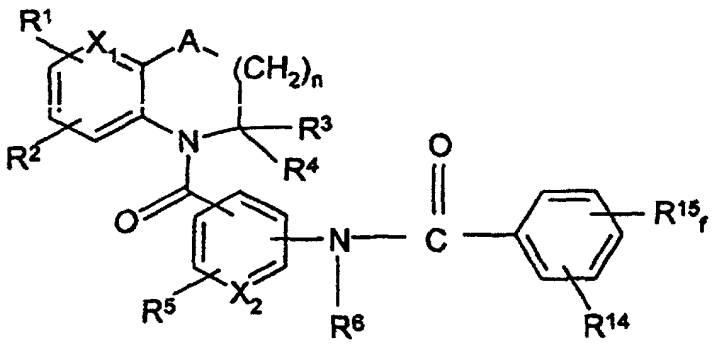
$R^7{}_h$ is (C_1-C_6)alkyl substituted with carboxy or N-[carboxy (C_1-C_6) alkyl]piperazinyl-carbonyl, or

j) reacting a compound of the formula:



(Ip)

or its reactive derivative at the carboxy group or a salt thereof with a hydroxy compound to provide a compound of the formula:

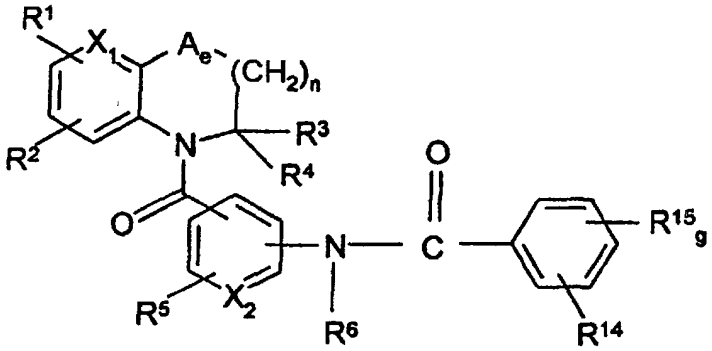


(Iq)

or its salt, in the above formulas,

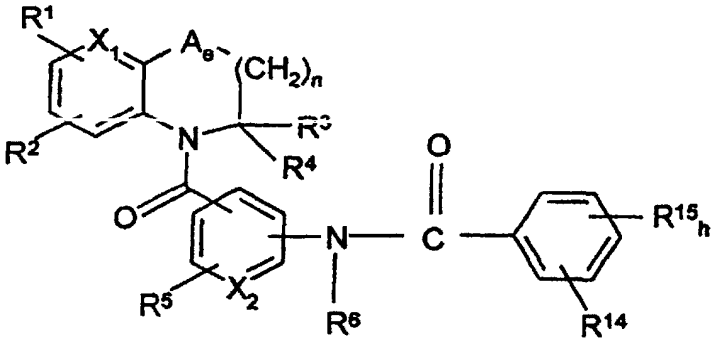
R^1, R^2, R^3, R^4, R^5, R^6, R^{14}, A, X_1, X_2 and n	are each as defined above,
$R^{15}{}_e$	is phenyl substituted with carboxy, and
$R^{15}{}_f$	is phenyl substituted with (C_1-C_6)alkoxycarbonyl, di(C_1-C_6)alkylamino(C_1-C_6)alkoxycarbonyl, halo(C_1-C_6)alkoxycarbonyl, trihalo(C_1-C_6)alkoxycarbonyl, phenoxycarbonyl, nitrophenoxycarbonyl, naphthyloxycarbonyl, phenyl(C_1-C_6)alkoxycarbonyl or nitrophenyl(C_1-C_6)alkoxycarbonyl, or

k) reacting a compound of the formula:



(Ir)

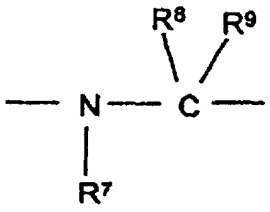
or its salt with a reducing agent to provide a compound of the formula:



(Is)

or its salt, in the above formulas,

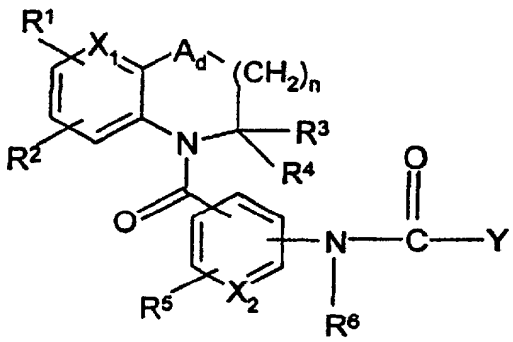
R^1, R^2, R^3, R^4, R^5, R^6, R^{14}, X_1, X_2 and n	are each as defined above,
A_e	is



in which

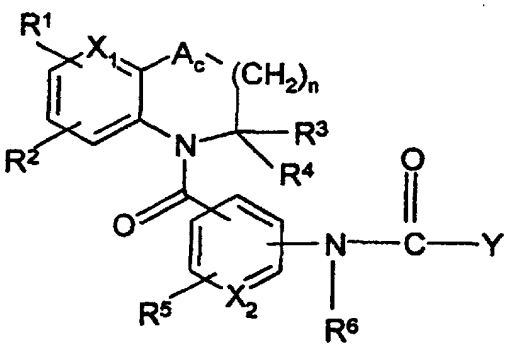
R^7, R^8 and R^9	are each as defined above,
$R^{15}{}_g$	is phenyl substituted with carboxy or (C_1-C_6)alkoxycarbonyl, and
$R^{15}{}_h$	is phenyl substituted with hydroxymethyl, or

l) reacting a compound of the formula:



(Io)

or its reactive derivative at the carboxy group or a salt thereof with a hydroxy compound to provide a compound of the formula:

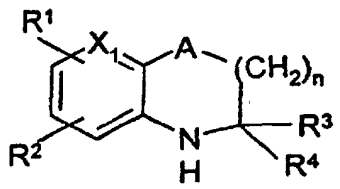


(In)

or its salt, in the above formulas,

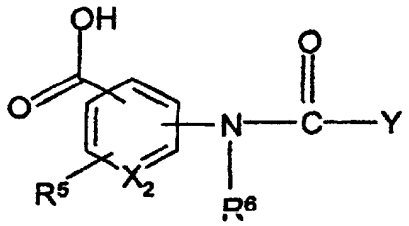
R^1, R^2, R^3, R^4, R^5, R^6, A_c, A_d, X_1, X_2, Y and n are each as defined above, or

m) reacting a compound of the formula:



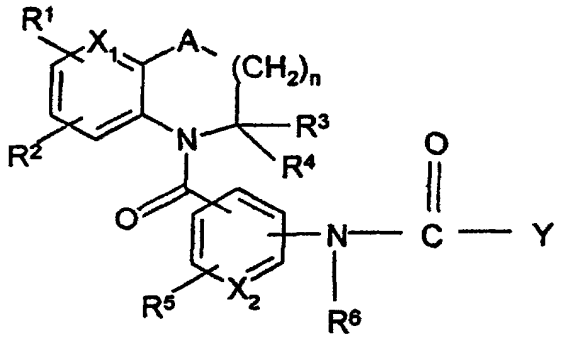
(IV)

or its salt with a compound of the formula:



(V)

or its reactive derivative at the carboxy group or a salt thereof to provide a compound of the formula:

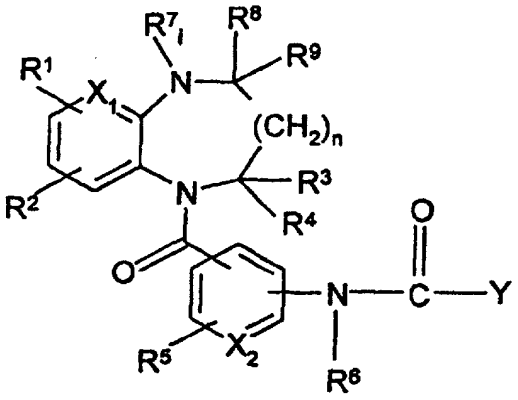


(I)

or its salt, in the above formulas,

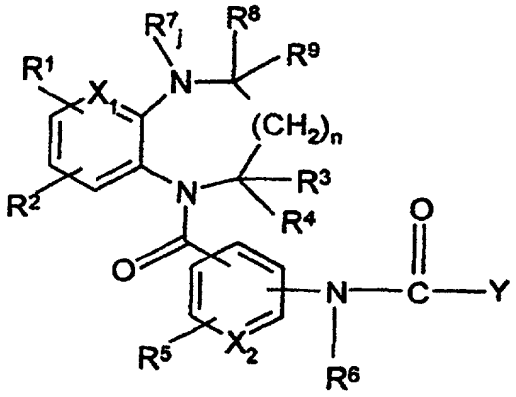
R^1, R^2, R^3, R^4, R^5, R^6, A, X_1, X_2, Y and n are each as defined above, or

n) subjecting a compound of the formula:



(It)

or its salt,
to elimination reaction of hydroxy protective group to provide a compound of the formula:

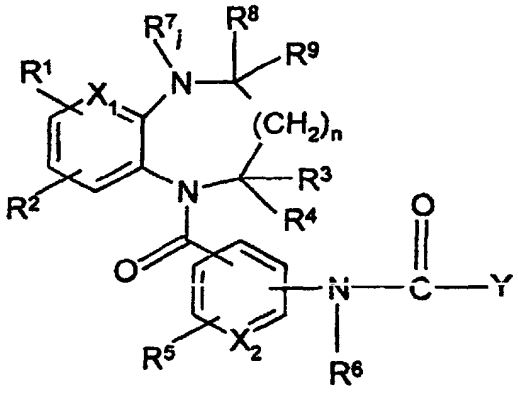


(Iu)

or its salt, in the above formulas,

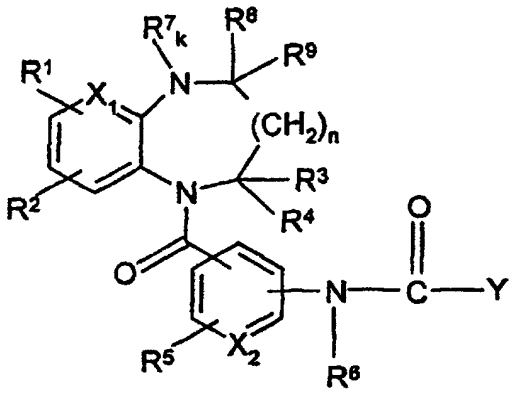
R^1, R^2, R^3, R^4, R^5, R^6, R^8, R^9, X_1, X_2, Y and n	are ach as defined above,
R^7i	is $(C_1$-$C_6)$alkyl substituted with $(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkoxy, phenyl$(C_1$-$C_6)$alkoxy, nitrophenyl$(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$alkanoyloxy, benzoyloxy, fluorenecarbonyloxy, $(C_1$-$C_6)$alkoxycarbonyloxy, phenyl$(C_1$-$C_6)$alkoxycarbonyloxy, halophenyl$(C_1$-$C_6)$alkoxycarbonyloxy or tri$(C_1$-$C_6)$alkylsilyloxy, and
R^7j	is $(C_1$-$C_6)$alkyl substituted with hydroxy, or

p) reacting a compound of the formula:



(Iu)

or its salt with an oxidizing agent to provide a compound of the formula:

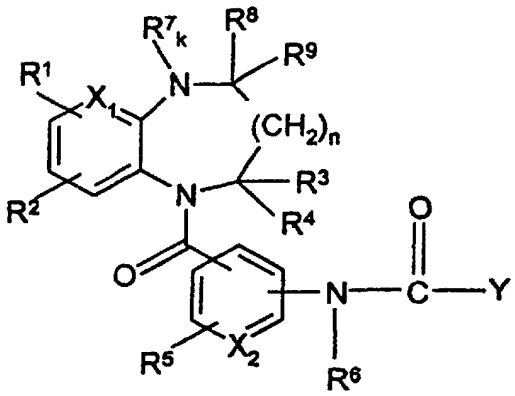


(Ix)

or its salt, in the above formulas,

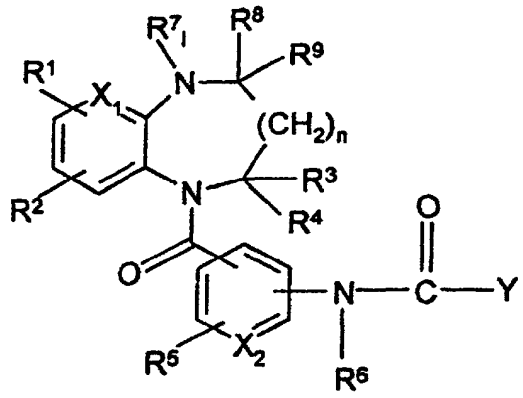
R^1, R^2, R^3, R^4, R^5, R^6, R^7_j, R^8, R^9, X_2, Y and n are each as defined above, and R^7_k is $(C_1$-$C_6)$alkyl substituted with formyl, or

q) reacting a compound of the formula:



(Ix)

or its salt with di $(C_1$-$C_6)$alkylamine, piperidine or N-$(C_1$-$C_6)$alkylpiperazine in the presence of a reducing agent to provide a compound of formula:



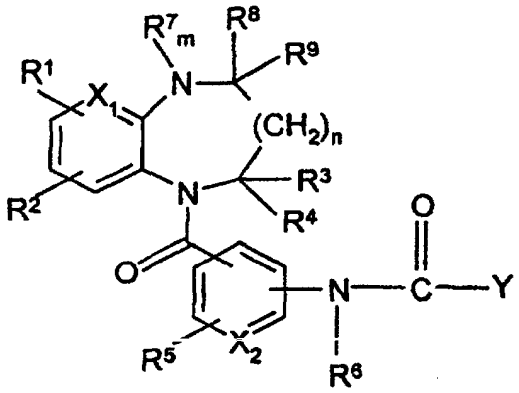
(Iy)

or its salt, in the above formulas,

R^1, R^2, R^3, R^4, R^5, R^6, R^7k, R^8, R^9, X_1, X_2, Y and n are each as defined above, and
R_l is (C_1-C_6)alkyl substituted with di (C1-C6)alkylamino, piperidyl or N-(C_1-C_6)alkylpiperazinyl,

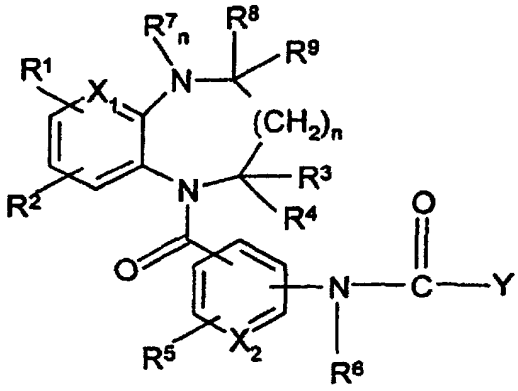
or

r) subjecting a compound of the formula:



(Iz)

or its salt to acylation reaction to provide a compound of the formula:

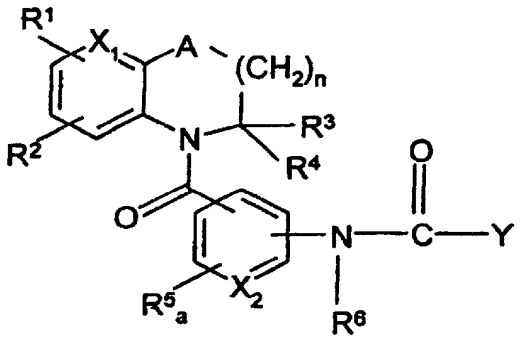


(I-1)

or its salt, in the above formulas,

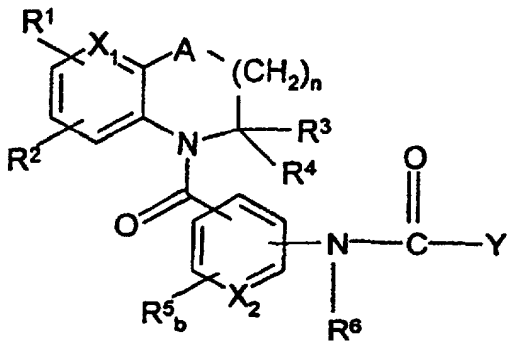
R^1, R^2, R^3, R^4, R^5, R^6, R^8, R^9, X_1, X_2, Y and n are each as defined above,
$R^7{}_m$ is (C_1-C_6)alkyl substituted with N-[hydroxy(C_1-C_6)alkyl] piperazinylcarbonyl, and
$R^7{}_n$ is (C_1-C_6)alkyl substituted with N-(C_1-C_6)alkanoyloxy (C_1-C_6)alkyl]piperazinylcarbonyl, or

t) reacting a compound of the formula:



(I-4)

or its salt with (C_1-C_6)alkyl halide or its salt, (C_1-C_6)alkyl in which may be substituted with (C_1-C_6)alkylamino, in the presence of a base to provide a compound.of the formula:

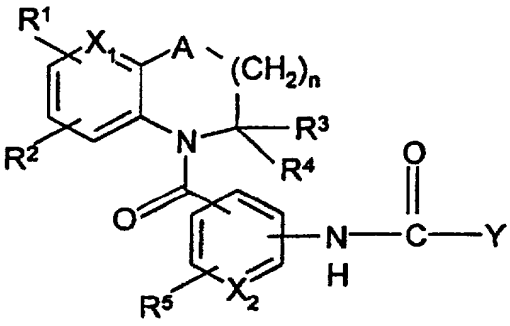


(I-5)

or its salt, in the above formulas,

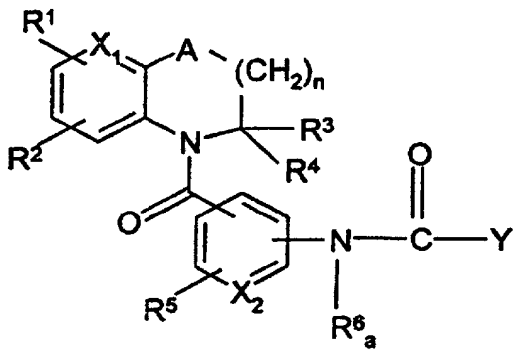
R^1, R^2, R^3, $R.^4$, R^6, A, X_1, X_2, Y and n	are each as defined above,
$R^5{}_a$	is hydroxy, and
$R^5{}_b$	is (C_1-C_6)alkoxy optionally substituted with (C_1-C_6)alkylamino, or

u) reacting a compound of the formula :



(Ia)

or its salt with an alkylating or acylating agent to provide a.compound of the formula:

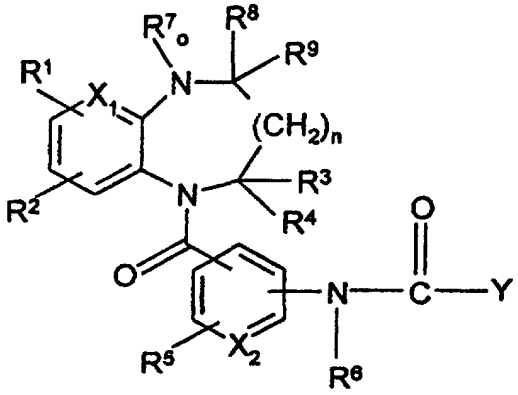


(I-6)

or its salt, in the above formulas,

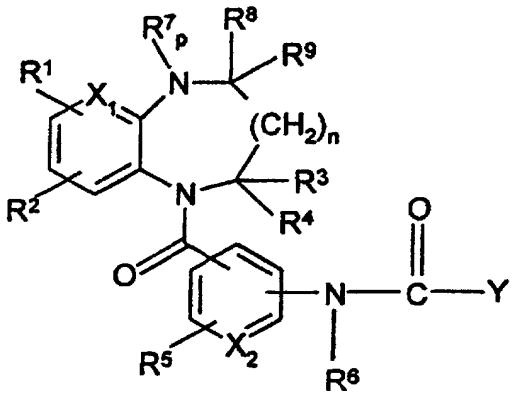
R^1, R^2, R^3, R^4, R^5, A, X_1, X_2, Y and n are each as defined above, and
$R^6{}_a$ is (C_1-C_6)alkyl or (C_1-C_6)alkoxycarbonyl, or

v) reacting a compound of the formula:



(I-7)

or its salt with (C_1-C_6)alkyl halide to provide a compound of the formula :



(I-8)

or its salt, in the above formulas,

R^1, R^2, R^3, R^4, R^5, R^6, R^8, R^9, X_1, X_2, Y and n	are each as defined above,
$R^7{}_o$	is (C_1-C_6)alkyl substituted with N-(C_1-C_6)alkylpiperazinylcarbonyl, and
$R^7{}_p$	is (C_1-C_6)alkyl substituted with N,N-di(C_1-C_6)alkyl)piperaziniocarbonyl.

8. A pharmaceutical composition comprising a compound of claim 1, as an active ingredient, in association with a pharmaceutically acceptable, substantially non-toxic carrier or excipient.

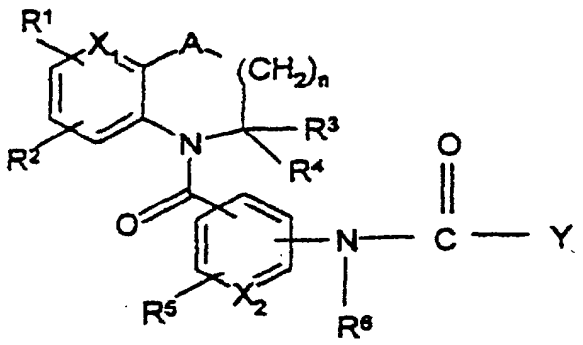
9. A compound of claim 1 for use as a medicament.

10. A compound of claims 1 for use in the treatment and/or prevention of hypertension, heart failure, renal insufficiency, edema, ascites, vasopressin parasecretion syndrome, hepatocirrhosis, hyponatremia, hypokalemia, diabetic or circulation disorder.

11. Use of a compound of claim 1 for the manufacture of a medicament for treating and/or preventing hypertension, heart failure, renal insufficiency, edema, ascites, vasopressin parasecretion syndrome, hepatocirrhosis, hyponatremia, hypokalemia, diabetic or circulation disorder in human beings or animals.

Patentansprüche

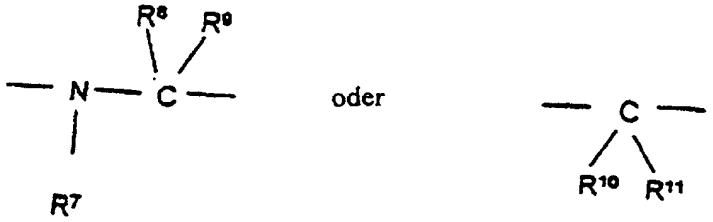
1. Verbindung der Formel:



(I)

worin

R^1 Wasserstoff oder (C_1-C_6) Alkyl ist,
R^2 Wassertoff, (C_1-C_6) Alkyl, Halogen (C_1-C_6) alkyl, Halogen oder (C_1-C_6) Alkoxy ist,
R^3 und R^4 jeweils Hydrogen, (C_1-C_6) Alkyl sind oder zusammengefasst werden, um ein Oxo zu bilden,
R^5 Wasserstoff, Halogen, Nitro, Hydroxy, (C_1-C_6) Alkoxy (C_1-C_6) alkoxy, (C_1-C_6) Alkoxy (C_1-C_6) alkoxy (C_1-C_6) alkoxy, Phenyl (C_1-C_6) alkoxy, Nitrophenyl (C_1-C_6) alkoxy, (C_1-C_6) Alkanoyloxy, Benzoyloxy, Fluorencarbonyloxy, (C_1-C_6) Alkoxycarbonyloxy, Phenyl (C_1-C_6) alkoxycarbonyloxy, Halogenphenyl (C_1-C_6) alkoxycarbonyloxy, Tri (C_1-C_6) alkylsilyloxy, (C_1-C_6) Alkyl oder (C_1-C_6) Alkoxy, das optional substituiert ist mit (C_1-C_6) Alkylamino, ist,
R^6 Wasserstoff, (C_1-C_6) Alkyl oder (C_1-C_6) Alkoxycarbonyl ist,
A ist



worin

R^7 ist Waserstoff; (C_1-C_6) Alkyl, das optional substituiert ist mit Halogen, Amino, (C_1-C_6) Alkylamino, (C_1-C_6) Alkanoylamino, Halogen (C_1-C_6) alkanoylamino, Phthaloylamino, (C_1-C_6) Alkoxycarbonylamino, Benzyloxycarbonylamino, Nitrobenzyloxycarbonylamino, Benzolsulfonylamino, Tosylamino, Nitrophenylsulfenylamino, Tritylamino, Benzylamino, Carboxy, (C_1-C_6) Alkoxycarbonyl, Di (C_1-C_6) alkylamino (C_1-C_6) alkoxycarbonyl, Halogen (C_1-C_6) Alkoxycarbonyl, Trihalogen (C_1-C_6) alkoxycarbonyl, Phenoxycarbonyl, Nitrophenoxycarbonyl, Naphthyloxycarbonyl, Phenyl (C_1-C_6) alkoxycarbonyl, Nitrophenyl (C_1-C_6) alkoxycarbonyl, Carbamoyl, (C_1-C_6) Alkylcarbamoyl, Trihalogen (C_1-C_6) alkanoyl, nicht substituiertes (C_1-C_6) Alkanoyl, Toluoyl, Di (tert-butyl) benzoyl, Tolylbenzoyl, Aminobenzoyl, Tolylbenzoylaminobenzoyl, nicht substituiertes Benzoyl, ein N-enthaltendes heterocyclisches Carbonyl, (C_1-C_6) Alkylsulfonyl, Tolylsulfonyl, Di (C_1-C_6) alkoxyphenylsulfonyl, nicht substituiertes Phenylsulfonyl, Piperidyl, Pyridyl, N- (C_1-C_6) Alkylpiperazinyl, Hydroxy, (C_1-C_6) Alkoxy (C_1-C_6) alkoxy, (C_1-C_6) Alkoxy (C_1-C_6) alkoxy (C_1-C_6) alkoxy, Phenyl (C_1-C_6) alkoxy, Nitrophenyl (C_1-C_6) alkoxy, (C_1-C_6) Alkanoyloxy, Benzoyloxy, Fluorencarbonyloxy, (C_1-C_6) Alkoxycarbonyloxy, Phenyl (C_1-C_6) alkoxycarbonyloxy, Halogenphenyl (C_1-C_6) alkoxycarbonyloxy, Tri (C_1-C_6) alkylsilyloxy oder Dimethoxyphenylsulfonyl; und

R^8 und R^9 zusammengenommen werden, um Oxo oder Thioxo zu bilden;

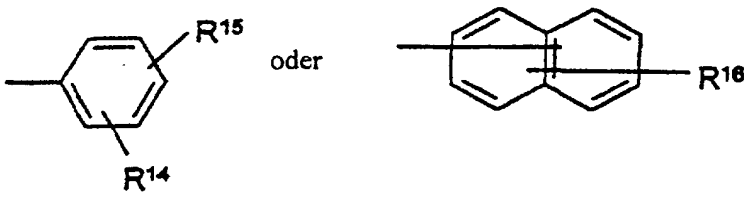
R^{10} Wasserstoff ist;

R^{11} Wasserstoff oder (C_1-C_6) Alkylamino ist;

X_1 CH ist,

X_2 CH oder N ist,

Y ist



worin

R^{14} Wasserstoff, Halogen, Hydroxy oder (C_1-C_6) Alkoxy ist,

R^{15} Phenoxy, Naphthyl, Phenyl, substituiert mit einem oder mehreren Substituenten, die aus der Gruppe ausgewählt sind, die besteht aus (C_1-C_6) Alkyl, (C_1-C_6) Alkoxy, Halogen, Halogen (C_1-C_6) alkyl, Hydroxy, Amino (C_1-C_6) alkyl, Azido (C_1-C_6) alkyl, (C_1-C_6) Alkylamino (C_1-C_6) alkyl, (C_1-C_6) Alkanoylamino (C_1-C_6) alkyl, Hydroxy (C_1-C_6) alkyl, Cyano, Carboxy, (C_1-C_6) Alkoxycarbonyl, Di (C_1-C_6) alkylamino (C_1-C_6) alkoxycarbonyl, Halogen (C_1-C_6) alkoxycarbonyl, Trihalogen (C_1-C_6) alkoxycarbonyl, Phenoxycarbonyl, Nitrophenoxycarbonyl, Naphthyloxycarbonyl, Phenyl (C_1-C_6) alkoxycarbonyl, Nitrophenyl (C_1-C_6) alkoxycarbonyl, Pyridyl oder Pyrrolyl ist, und

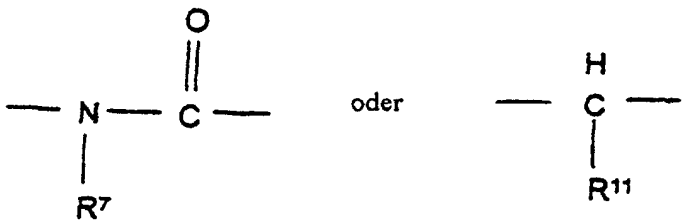
R^{16} Tolyl ist und

n 0, 1, 2 oder 3 ist,

und pharmazeutisch akzeptable Salze davon.

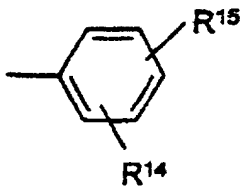
2. Verbindung nach Anspruch 1, worin

R^1 Wasserstoff ist,
R^2 Wasserstoff, (C_1-C_6) Alkyl oder Halogen ist,
R^3 Wasserstoff ist,
R^4 Wasserstoff ist,
R^5 Wasserstoff oder (C_1-C_6) Alkoxy ist,
R^6 Wasserstoff ist,
A ist



worin

R^7 Wasserstoff oder (C_1-C_6) Alkyl ist, das optional substituiert ist mit Amino, (C_1-C_6) Alkylamino, (C_1-C_6) Alkanoylamino, Halogen (C_1-C_6) alkanoylamino, Phthaloylamino, (C_1-C_6) Alkoxycarbonylamino, Benzyloxycarbonylamino, Nitrobenzyloxycarbonylamino, Benzolsulfonylamino, Tosylamino, Nitrophenylsulfenylamino, Tritylamino, Benzylamino, Carboxy, (C_1-C_6) Alkoxycarbonyl, Di (C_1-C_6) alkylamino (C_1-C_6) alkoxycarbonyl, Halogen (C_1-C_6) alkoxycarbonyl, Trihalogen (C_1-C_6)alkoxycarbonyl, Phenoxycarbonyl, Nitrophenoxycarbonyl, Naphthyloxycarbonyl, Phenyl (C_1-C_6) alkoxycarbonyl, Nitrophenyl (C_1-C_6) alkoxycarbonyl, Carbamoyl, (C_1-C_6) alkylcarbamoyl, Trihalogen (C_1-C_6) alkanoyl, nicht substituiertes (C_1-C_6) Alkanoyl, Toluoyl, Di (tert-Butyl) benzoyl, Tolylbenzoyl, Aminobenzoyl, Tolylbenzoylaminobenzoyl, nicht substituiertes Benzoyl, ein N-enthaltendes heterocyclisches Carbonyl, (C_1-C_6) Alkylsulfonyl, Tolylsulfonyl, Di (C_1-C_6) alkoxyphenylsulfonyl, nicht substituiertes Phenylsulfonyl, Piperidyl, Pyridyl, N-(C_1-C_6) Alkylpiperazinyl; und
R^{11} Wasserstoff oder (C_1-C_6) Alkylamino ist,
X_1 CH ist,
X_2 CH ist,
Y ist

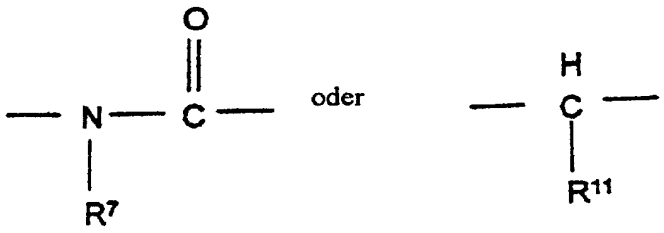


worin

R^{14} und R^{15} sowie oben definiert sind, und
n 0, 1 oder 2 ist.

3. Verbindung nach Anspruch 2, worin

A ist



worin

R^7 ein niederes Alkyl ist, welches optional substituiert ist mit Amino, (C_1-C_6)Alkylamino, (C_1-C_6) Alkanoylamino, Halogen (C_1-C_6) alkanoylamino, Phthaloylamino, (C_1-C_6) Alkoxycarbonylamino, Benzyloxycarbonylamino, Nitrobenzyloxycarbonylamino, Benzolsulfonylamino, Tosylamino, Nitrophenylsulfenylamino, Tritylamino, Benzylamino, Carboxy, (C_1-C_6) Alkoxycarbonyl, Di (C_1-C_6) alkylamino (C_1-C_6) alkoxycarbonyl, Halogen (C_1-C_6) alkoxycarbonyl, Trihalogen (C_1-C_6) alkoxycarbonyl, Phenoxycarbonyl, Nitrophenoxycarbonyl, Naphthyloxycarbonyl, Phenyl (C_1-C_6) alkoxycarbonyl, Nitrophenyl (C_1-C_6) alkoxycarbonyl, Carbamoyl, (C_1-C_6) Alkylcarbamoyl, Trihalogen (C_1-C_6) alkanoyl, nicht substituiertes (C_1-C_6) Alkanoyl, Toluoyl, Di(tert-butyl) benzoyl, Tolylbenzoyl, Aminobenzoyl, Tolylbenzoylaminobenzoyl, nicht substituiertes Benzoyl, ein N-enthaltendes heterocyclisches Carbonyl, (C_1-C_6) Alkylsulfonyl, Tolylsulfonyl, Di (C_1-C_6) alkoxyphenylsulfonyl, nicht substituiertes Phenylsulfonyl oder Piperidino; und

R^{11} Wasserstoff oder (C_1-C_6) Alkylamino ist und

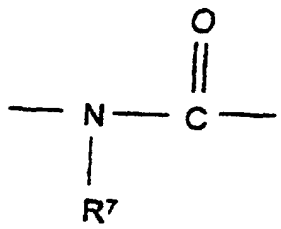
Y ist

worin

R^{15} Phenyl ist, das mit einem oder mehreren Substituenten substituiert ist, die aus der Gruppe ausgewählt sind, die besteht aus (C_1-C_6) Alkyl, (C_1-C_6) Alkoxy, Halogen, Halogen (C_1-C_6) alkyl, Hydroxy, Amino (C_1-C_6) alkyl, Azido (C_1-C_6) alkyl, (C_1-C_6) Alkylamino (C_1-C_6) alkyl, (C_1-C_6) Alkanoylamino (C_1-C_6) alkyl, Hydroxy (C_1-C_6) alkyl, Cyano, Carboxy, (C_1-C_6) Alkoxycarbonyl, Di (C_1-C_6) alkylamino (C_1-C_6) alkoxycarbonyl, Halogen (C_1-C_6) alkoxycarbonyl, Trihalogen (C_1-C_6) alkoxycarbonyl, Phenoxycarbonyl, Nitrophenoxycarbonyl, Naphthyloxycarbonyl, Phenyl (C_1-C_6) alkoxycarbonyl und Nitrophenyl (C_1-C_6) alkoxycarbonyl.

4. Verbindung nach Anspruch 3, worin

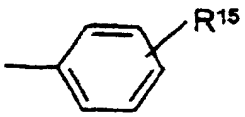
A ist



worin

R^7 ist (C_1-C_6) Alkyl, das substituiert ist mit N- (C_1-C_6) Alkylpiperazinylcarbonyl, oder (C_1-C_6) Alkyl, das substituiert ist mit Di (C_1-C_6) alkylamino, und

Y ist

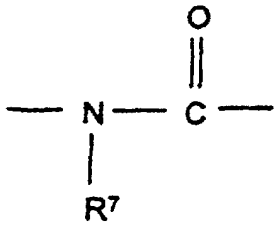


worin

R^{15} ein Phenyl ist, das substituiert ist mit (C_1-C_6) Alkyl oder Di (C_1-C_6) alkyl.

5. Verbindung nach Anspruch 4, worin

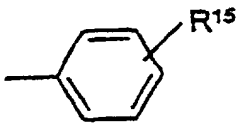
R^2 Wasserstoff ist,
R^5 Wasserstoff ist,
A ist



worin

R^7 (C_1-C_6) Alkyl ist, das substituiert ist mit N- (C_1-C_6) alkylpiperazinylcarbonyl,

Y ist

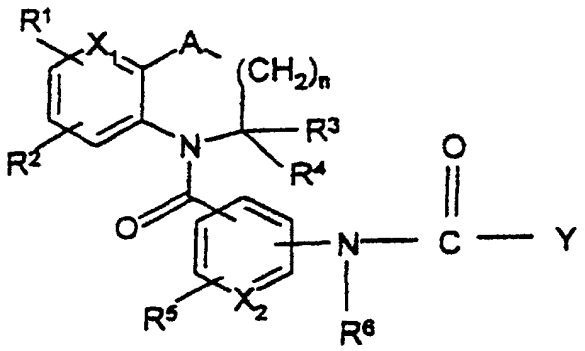


worin

R^{15} Phenyl ist, das substituiert ist mit (C_1-C_6) Alkyl oder mit Di (C_1-C_6) alkyl und
n 1 ist.

6. Verbindung nach Anspruch 5, die 5-{4-[2-(4-Methylphenyl)benzoylamino]benzoyl}-1-[(4-methyl-1-piperazinyl)carbonylmethyl]-1,3,4,5-tetrahydro-1,5-benzodiazepin-2(2H)-on ist.

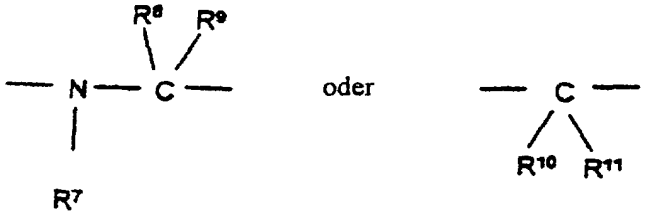
7. Verfahren zur Herstellung einer Verbindung der Formel



(I)

worin

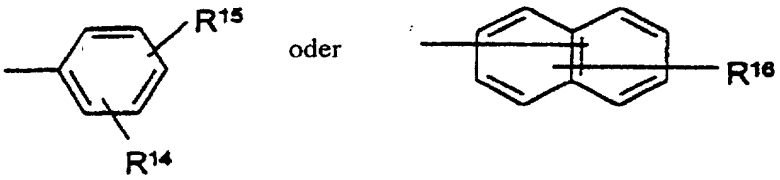
R^1	Wasserstoff oder (C_1-C_6)Alkyl ist,
R^2	Wassertoff, (C_1-C_6) Alkyl, Halogen (C_1-C_6) Alkyl, Halogen oder (C_1-C_6) Alkoxy ist,
R^3 und R^4	jeweils Hydrogen, (C_1-C_6) Alkyl sind oder zusammengefasst werden, um ein Oxo zu bilden,
R^5	Wasserstoff, Halogen, Nitro, Hydroxy, (C_1-C_6) Alkoxy (C_1-C_6) alkoxy, (C_1-C_6) Alkoxy (C_1-C_6) alkoxy (C_1-C_6) alkoxy, Phenyl (C_1-C_6) alkoxy, Nitrophenyl (C_1-C_6) alkoxy, (C_1-C_6) Alkanoyloxy, Benzoyloxy, Fluorencarbonyloxy, (C_1-C_6) Alkoxycarbonyloxy, Phenyl (C_1-C_6) alkoxycarbonyloxy, Halogenphenyl (C_1-C_6) alkoxycarbonyloxy, Tri (C_1-C_6) alkylsilyloxy, (C_1-C_6) Alkyl oder (C_1-C_6) Alkoxy ist, das optional substituiert ist mit (C_1-C_6) Alkylamino,
R^6	Wasserstoff, (C_1-C_6) Alkyl oder (C_1-C_6) Alkoxycarbonyl ist,
A	ist



worin

R^7	ist Wasserstoff; (C_1-C_6) Alkyl, das optional substituiert ist mit Halogen, Amino, (C_1-C_6) Alkylamino, (C_1-C_6) Alkanoylamino, Halogen (C_1-C_6) alkanoylamino, Phthaloylamino, (C_1-C_6) Alkoxycarbonylamino, Benzyloxycarbonylamino, Nitrobenzyloxycarbonylamino, Benzolsulfonylamino, Tosylamino, Nitrophenylsulfenylamino, Tritylamino, Benzylamino, Carboxy, (C_1-C_6) Alkoxycarbonyl, Di (C_1-C_6) alkylamino (C_1-C_6) alkoxycarbonyl, Halogen (C_1-C_6) Alkoxycarbonyl, Trihalogen (C_1-C_6) alkoxycarbonyl, Phenoxycarbonyl, Nitrophenoxycarbonyl, Naphthyloxycarbonyl, Phenyl (C_1-C_6) alkoxycarbonyl, Nitrophenyl (C_1-C_6) alkoxycarbonyl, Carbamoyl, (C_1-C_6) Alkylcarbamoyl, Trihalogen (C_1-C_6) alkanoyl, nicht substituiertes (C_1-C_6) Alkanoyl, Toluoyl, Di (tert-Butyl) benzoyl, Tolylbenzoyl, Aminobenzoyl, Tolylbenzoylaminobenzoyl, nicht substituiertes Benzoyl, ein N-enthaltendes heterocyclisches Carbonyl, (C_1-C_6) Alkylsulfonyl, Tolylsulfonyl, Di (C_1-C_6) alkoxyphenylsulfonyl, nicht substituiertes Phenylsulfonyl, Piperidyl, Pyridyl, N- (C_1-C_6) Alkylpiperazinyl, Hydroxy, (C_1-C_6) Alkoxy (C_1-C_6) alkoxy, (C_1-C_6) Alkoxy (C_1-C_6) alkoxy (C_1-C_6) alkoxy, Phenyl (C_1-C_6) alkoxy, Nitrophenyl (C_1-C_6) alkoxy, (C_1-C_6) Alkanoyloxy, Benzoyloxy, Fluorencarbonyloxy, (C_1-C_6) Alkoxycarbonyloxy, Phenyl (C_1-C_6) alkoxycarbonyloxy, Halogenphenyl (C_1-C_6) alkoxycarbonyloxy, Tri (C_1-C_6) alkylsilyloxy oder Dimethoxyphenylsulfonyl; und
R^8 und R^9	zusammengenommen werden, um Oxo oder Thioxo zu bilden;
R^{10}	Wasserstoff ist;
R^{11}	Wasserstoff oder (C_1-C_6) Alkylamino ist;
X_1	CH ist,

X_2 CH oder N ist,
Y ist

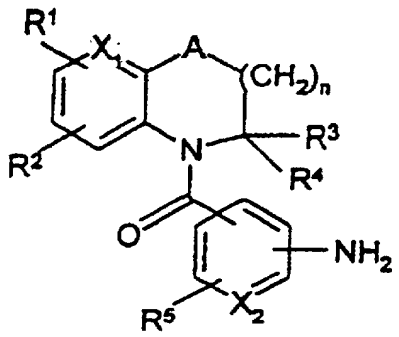


worin

R^{14} Wasserstoff, Halogen, Hydroxy oder (C_1-C_6) Alkoxy ist,
R^{15} Phenoxy, Naphthyl, Phenyl, substituiert mit einem oder mehreren Substituenten, die aus der Gruppe ausgewählt sind, die besteht aus (C_1-C_6) Alkyl, (C_1-C_6) Alkoxy, Halogen, Halogen (C_1-C_6) alkyl, Hydroxy, Amino (C_1-C_6) alkyl, Azido (C_1-C_6) alkyl, (C_1-C_6) Alkylamino (C_1-C_6) alkyl, (C_1-C_6) Alkanoylamino (C_1-C_6) alkyl, Hydroxy (C_1-C_6) alkyl, Cyano, Carboxy, (C_1-C_6) Alkoxycarbonyl, Di (C_1-C_6) alkylamino (C_1-C_6) alkoxycarbonyl, Halogen (C_1-C_6) alkoxycarbonyl, Trihalogen (C_1-C_6) alkoxycarbonyl, Phenoxycarbonyl, Nitrophenoxycarbonyl, Naphthyloxycarbonyl, Phenyl (C_1-C_6) alkoxycarbonyl, Nitrophenyl (C_1-C_6) alkoxycarbonyl, Pyridyl oder Pyrrolyl ist, und
R^{16} Tolyl ist und
n 0, 1, 2 oder 3 ist,

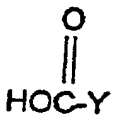
oder Salze davon, wobei das Verfahren umfasst,

a) Reaktion einer Verbindung der Formel:



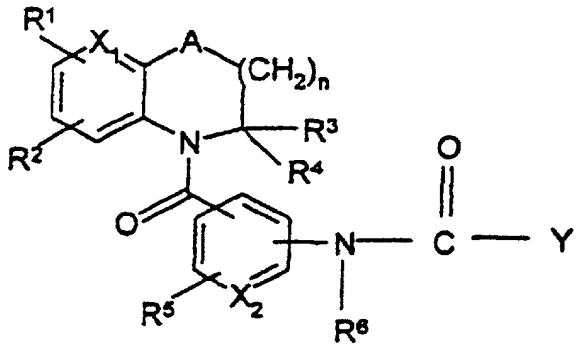
(II)

oder ihres Salzes mit einer Verbindung der Formel:



(III)

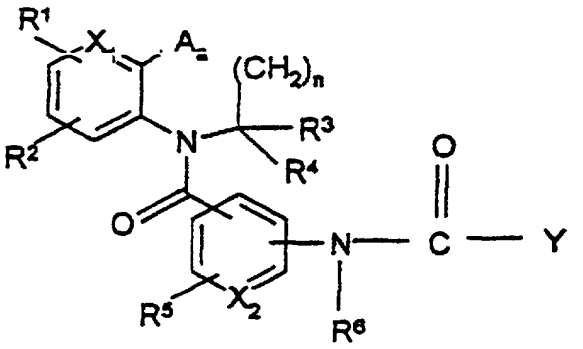
oder ihr reaktives Derivat an der Carboxygruppe oder ein Salz davon, um eine Verbindung der Formel:



(Ia)

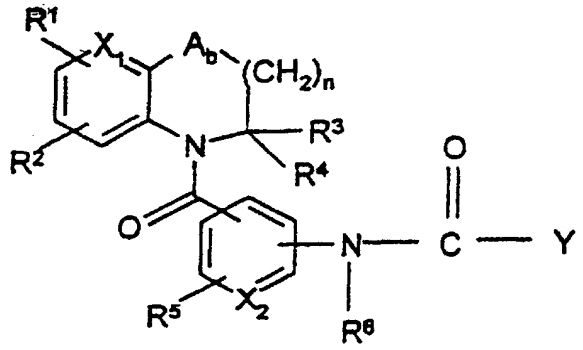
oder ihr Salz bereitzustellen, wobei in den obigen Formeln R^1, R^2, R^3, R^4, R^5, A, X_1, X_2, Y und n jeweils wie oben definiert sind, oder

b) Reaktion einer Verbindung der Formel:



(Ib)

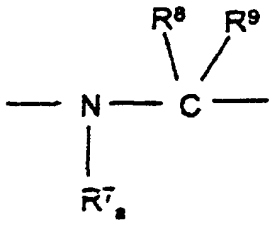
oder ihr reaktives Derivat an der Carboxygruppe oder ein Salz davon mit einem Amin, um eine Verbindung der Formel:



(Ic)

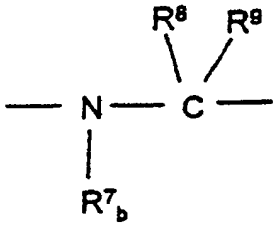
oder ihr Salz bereitzustellen, wobei in den obigen Formeln R^1, R^2, R^3, R^4, R^5, R^6, X_1, X_2,Y und n jeweils so wie oben definiert sind,

A_a ist



worin

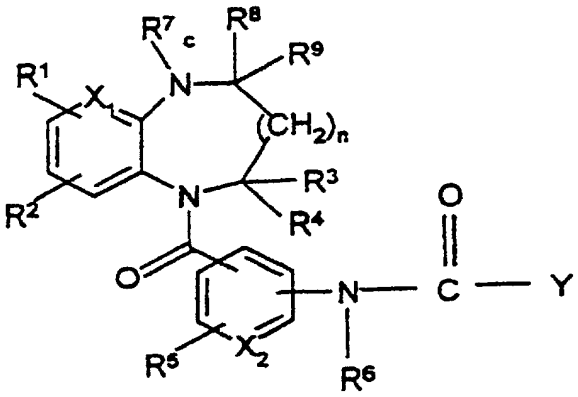
R^8 und R^9 jeweils wie oben definiert sind;
$R^7{}_a$ ist ein (C_1-C_6) Alkyl, das mit Carboxy substituiert ist, und
A_b ist



worin

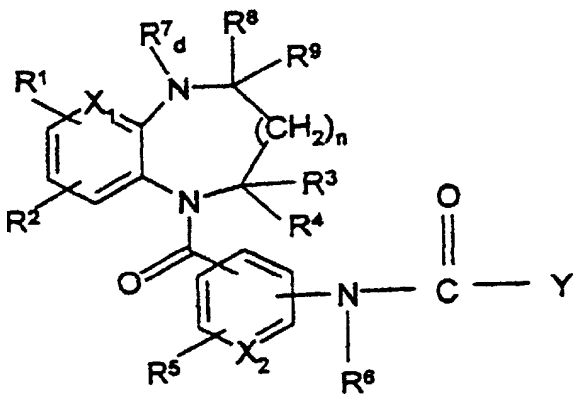
R^8 und R^9 jeweils so wie oben definiert sind;
$R^7{}_b$ ist ein (C_1-C_6) Alkyl, das mit Carbamoyl substituiert ist, welches mit (C_1-C_6) Alkyl substituiert sein kann, oder ein N-enthaltendes, heterocyclisches Carbonyl; oder

c) Unterwerfen einer Verbindung der Formel



(Id)

oder ihres Salzes unter eine Eliminierungsreaktion der N-Schutzgruppe, um eine Verbindung der Formel :



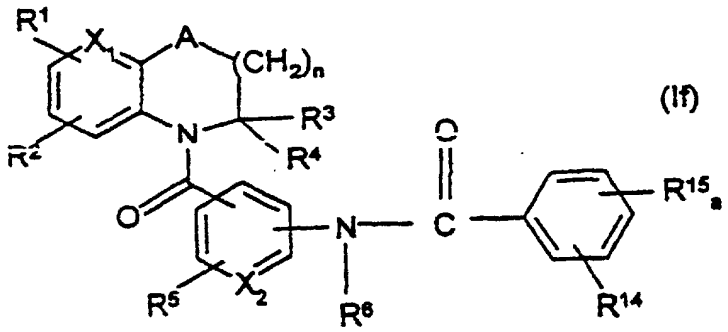
(Ie)

oder ihr Salz bereitzustellen, wobei in den obigen Formeln

R^1, R^2, R^3, R^4, R^5, R^6, R^8, R^9, X_1, X_2,Y und n	jeweils so wie oben definiert sind,
$R^7{}_c$	ist ein (C_1-C_6) Alkyl, das substituiert ist mit (C_1-C_6) Alkanoylamino, Halogen (C_1-C_6) alkanoylamino, Phthaloylamino, (C_1-C_6) Alkoxycarbonylamino, Benzyloxycarbonylamino, Nitrobenzyloxycarbonylamino, Benzolsulfonylamino, Tosylamino, Nitrophenylsulfenylamino, Tritylamino, Benzylamino oder N- (C_1-C_6) Alkoxycarbonylpiperazinylcarbonyl, und
$R^7{}_d$	ist ein (C_1-C_6) Alkyl, das substituiert ist mit Amino oder mit Piperazinylcarbonyl,

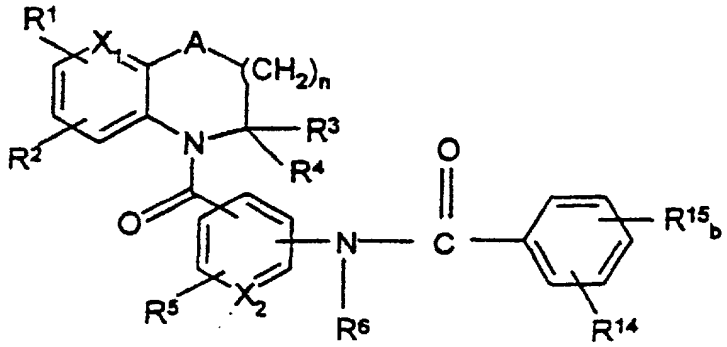
oder

d) Unterwerfen einer Verbindung der Formel:



(If)

oder ihres Salzes unter eine Reduktion, um eine Verbindung mit der Formel :

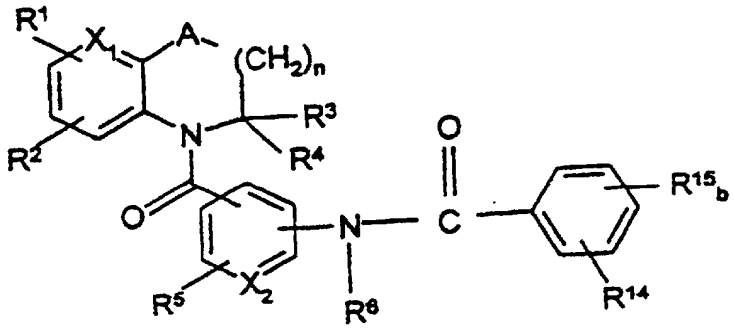


(Ig)

oder ihr Salz bereitzustellen, wobei in den obigen Formeln

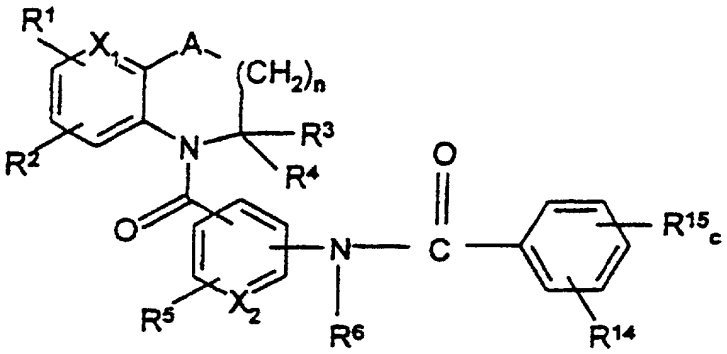
R^1, R^2, R^3, R^4, R^5, R^6, R^{14}, A, X_1, X_2 und n	jeweils so wie oben definiert sind,
$R^{15}{}_a$	ist ein Phenyl, das substituiert ist mit Azido (C_1-C_6) alkyl und
$R^{15}{}_b$	ist ein Phenyl, das substituiert ist mit Amino (C_1-C_6) alkyl, oder

e) Reaktion einer Verbindung der Formel:



(Ig)

oder ihres Salzes mit einem Acylierungsmittel, um eine Verbindung der Formel :

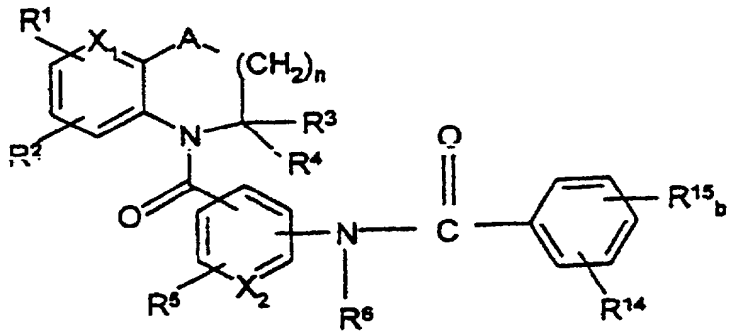


(Ih)

oder ihr Salz bereitzustellen, wobei in den obigen Formeln,

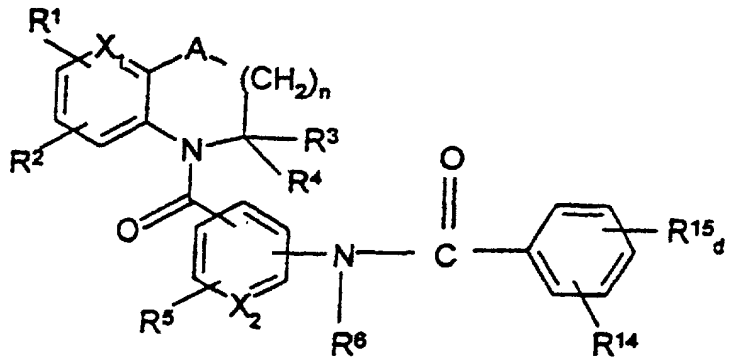
R^1, R^2, R^3, R^4, R^5, R^6, R^{14}, $R^{15}{}_b$, A, X_1, X_2 und n	jeweils so wie oben definiert sind, und
$R^{15}{}_c$	ist ein Phenyl, das substituiert ist mit (C_1-C_6) Alkanoyl-amino (C_1-C_6) alkyl,

f) Reaktion einer Verbindung der Formel:



(Ig)

oder ihres Salzes unter einem Alkylierungsmittel, um eine Verbindung der Formel :

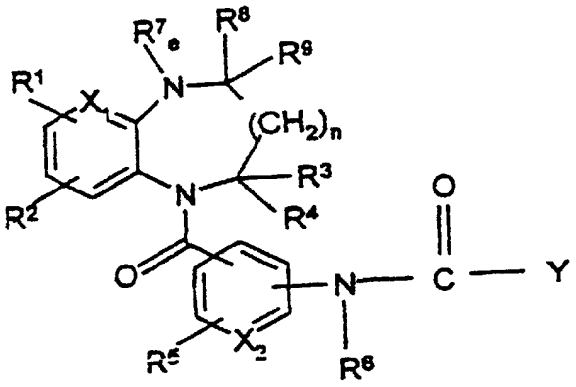


(Ii)

oder ihr Salz bereitzustellen, wobei in den obigen Formeln,

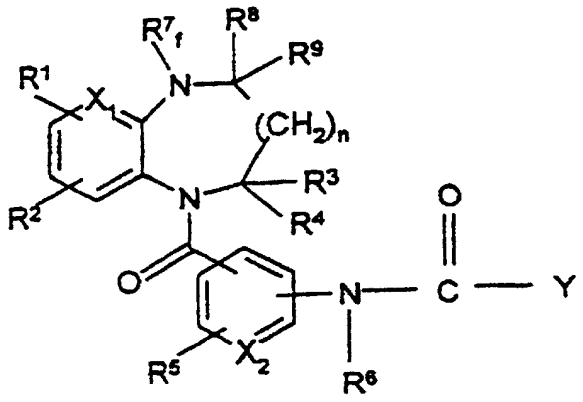
R^1, R^2, R^3, R^4, R^5, R^6, R^{14}, $R^{15}{}_b$, A, X_1, X_2 und n	jeweils so wie oben definiert sind, und
$R^{15}{}_d$	ist ein Phenyl, das substituiert ist mit (C_1-C_6) Alkylamino (C_1-C_6) alkyl, oder

g) Reaktion einer Verbindung der Formel:



(Ij)

oder ihres Salzes mit einem Alkylierungsmittel, um eine Verbindung der Formel :

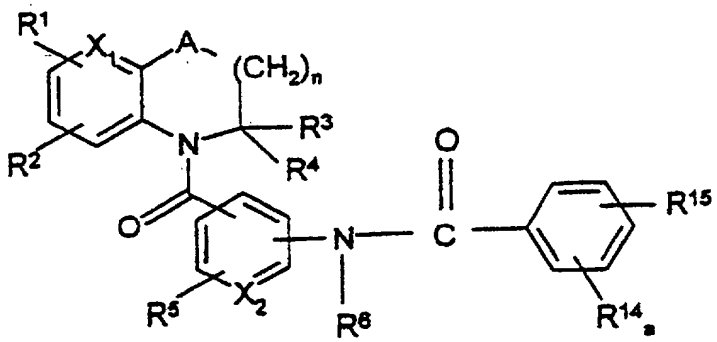


(Ik)

oder ihr Salz bereitzustellen, wobei in den obigen Formeln,

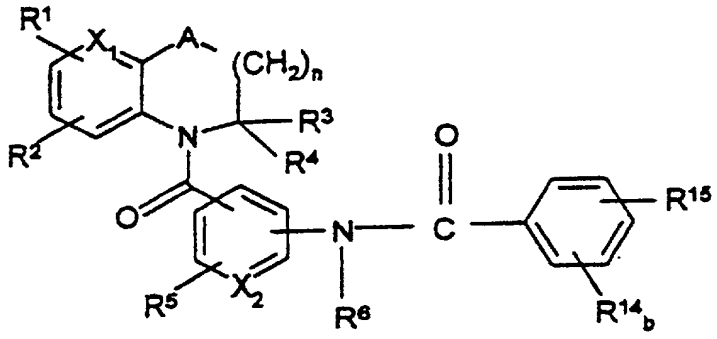
R^1, R^2, R^3, R^4, R^5, R^6, R^8, R^9, X_1, X_2, Y und n	jeweils so wie oben definiert sind,
$R^7{}_e$	ist (C_1-C_6) Alkyl, das substituiert ist mit einem Amino, und
$R^7{}_f$	ist (C_1-C_6) Alkyl, das substituiert ist mit (C_1-C_6) Alkylamino, oder

h) Unterwerfen einer Verbindung der Formel:



(Il)

oder ihres Salzes unter eine Dealkylierungsreaktion, um eine Verbindung der Formel:

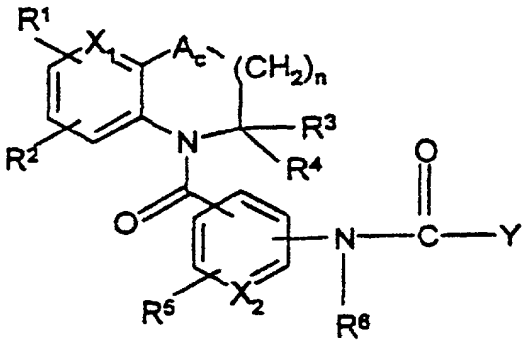


(Im)

oder ihr Salz bereitzustellen, wobei in den obigen Formeln,

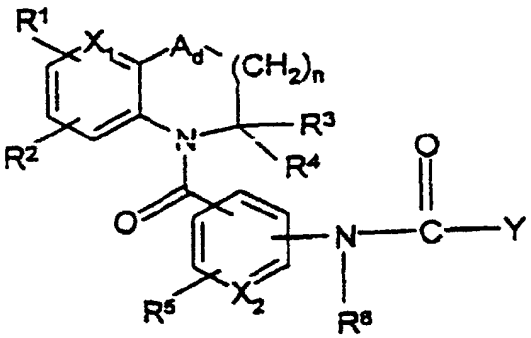
R^1, R^2, R^3, R^4, R^5, R^6, R^{15}, A, X_1, X_2, und n	jeweils so wie oben definiert sind,
$R^{14}{}_a$	ist ein (C_1-C_6) Alkoxy, und
$R^{14}{}_b$	ist ein Hydroxy, oder

i) Unterwerfen einer Verbindung der Formel:



(In)

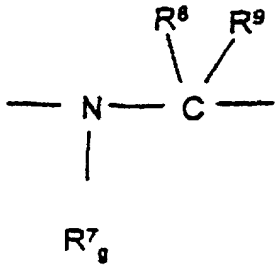
oder ihres Salzes unter einer Esterabspaltungsreaktion, um eine Verbindung der Formel :



(Io)

oder ihr Salz bereitzustellen, wobei in den obigen Formeln,

R^1, R^2, R^3, R^4, R^5, R^6, X_1, X_2, Y und n	jeweils so wie oben definiert sind,
A_c	ist

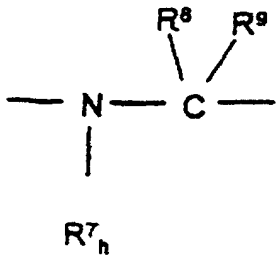


worin

R^8 und R^9	jeweils so wie oben definiert sind;
$R^7{}_g$	ist ein (C_1-C_6) Alkyl, das substituiert ist mit (C_1-C_6) Alkoxycarbonyl, Di (C_1-C_6) alkylamino

(C_1-C_6) alkoxycarbonyl, Halogen (C_1-C_6) alkoxycarbonyl, Trihalogen (C_1-C_6) alkoxycarbonyl, Phenoxycarbonyl, Nitrophenoxycarbonyl, Naphthyloxycarbonyl, Phenyl (C_1-C_6) alkoxycarbonyl, Nitrophenyl (C_1-C_6) alkoxycarbonyl oder N-[(C_1-C_6) Alkoxycarbonyl (C_1-C_6) alkyl]piperazinyl-carbonyl; und

A_d ist

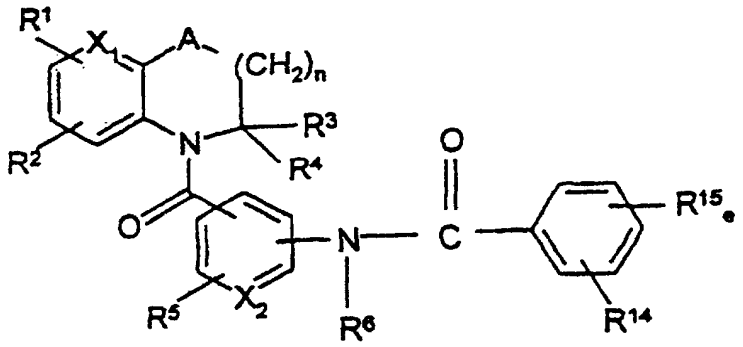


worin

R^8 und R^9 jeweils so wie oben definiert sind, und

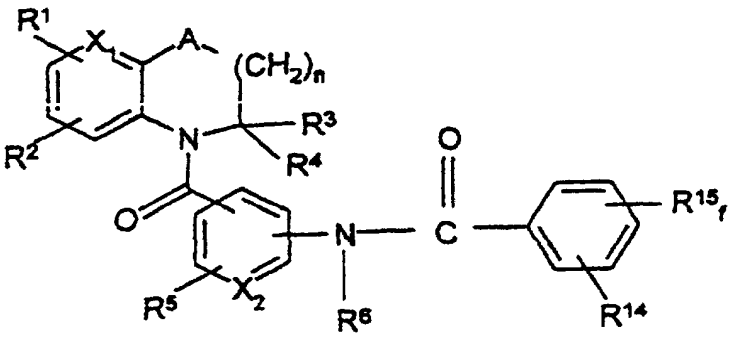
$R^7{}_h$ ist ein (C_1-C_6) Alkyl, das substituiert ist mit Carboxy oder mit N-[Carboxy (C_1-C_6) alkyl]piperazinylcarbonyl, oder

j) Reaktion einer Verbindung der Formel:



(Ip)

oder ihres reaktiven Derivates an der Carboxygruppe oder ein Salz davon mit einer Hydroxyverbindung, um eine Verbindung der Formel :

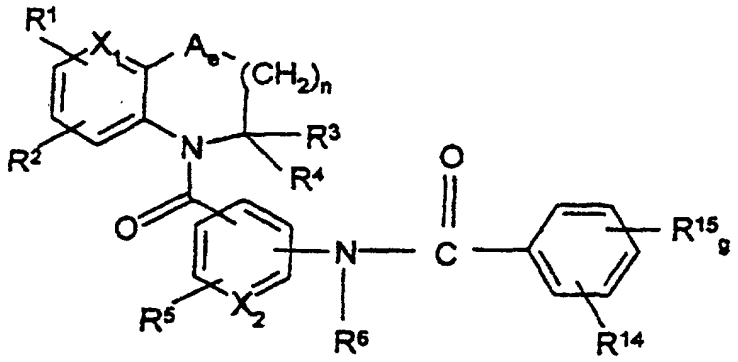


(Iq)

oder ihr Salz bereitzustellen, wobei in den obigen Formeln,

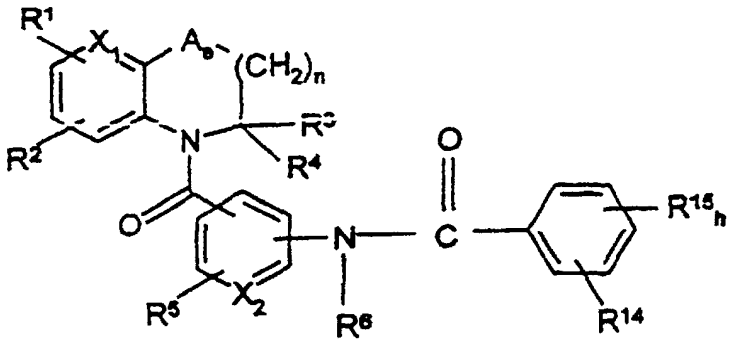
R^1, R^2, R^3, R^4, R^5, R^6, R^{14}, A, X_1, X_2, und n	jeweils so wie oben definiert sind, .
$R^{15}{}_e$	ist ein Phenyl, das mit Carboxy substituiert ist, und
$R^{15}{}_f$	ist ein Phenyl, das substituiert ist mit (C_1-C_6) Alkoxycarbonyl, Di (C_1-C_6) alkylamino (C_1-C_6) alkoxycarbonyl, Halogen (C_1-C_6) alkoxycarbonyl, Trihalogen (C_1-C_6) alkoxycarbonyl, Phenoxycarbonyl, Nitrophenoxycarbonyl, Naphthyloxycarbonyl, Phenyl (C_1-C_6) alkoxycarbonyl oder Nitrophenyl (C_1-C_6) alkoxycarbonyl, oder

k) Reaktion einer Verbindung der Formel:



(Ir)

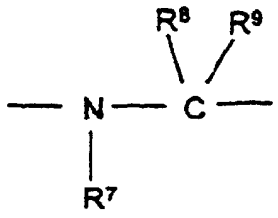
oder ihres Salzes mit einem Reduktionsmittel, um eine Verbindung der Formel:



(Is)

oder ihr Salz bereitzustellen, wobei in den obigen Formeln,

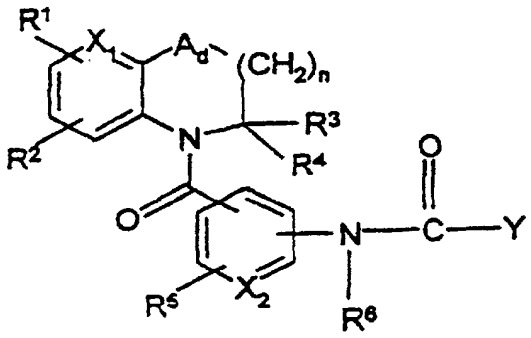
R^1, R^2, R^3, R^4, R^5, R^6, R^{14}, X_1, X_2, und n	jeweils so wie oben definiert sind,
A_c	ist



worin

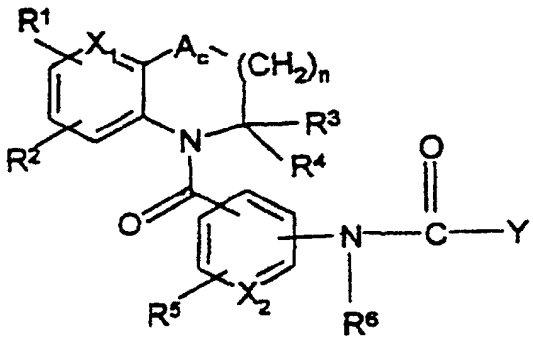
R^7, R^8 und R^9 jeweils so wie oben definiert sind,
$R^{15}{}_g$ ist ein Phenyl, das substituiert ist mit Carboxy oder (C_1-C_6) Alkoxycarbonyl, und
$R^{15}{}_h$ ist ein Phenyl, das mit Hydroxymethyl substituiert ist, oder

l) Reaktion einer Verbindung der Formel:



(Io)

oder ihres reaktiven Derivates an der Carboxygruppe oder ein Salz davon mit einer Hydroxyverbindung, um eine Verbindung der Formel :

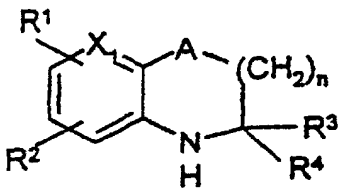


(In)

oder ihr Salz bereitzustellen, wobei in den obigen Formeln,

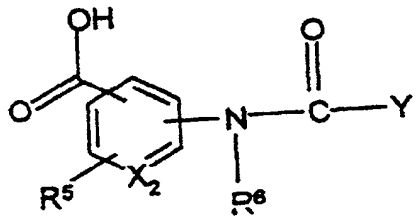
R^1, R^2, R^3, R^4, R^5, R^6, A_c, A_d, X_1, X_2, Y und n jeweils so wie oben definiert sind, oder

m) Reaktion einer Verbindung der Formel:



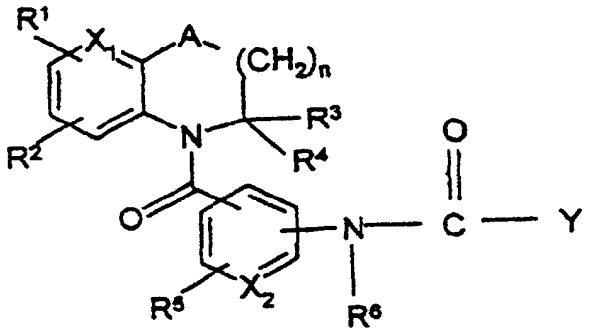
(IV)

oder ihres Salzes mit einer Verbindung der Formel:



(V)

oder ihres reaktiven Derivates an der Carboxygruppe oder ein Salz davon, um eine Verbindung der Formel:

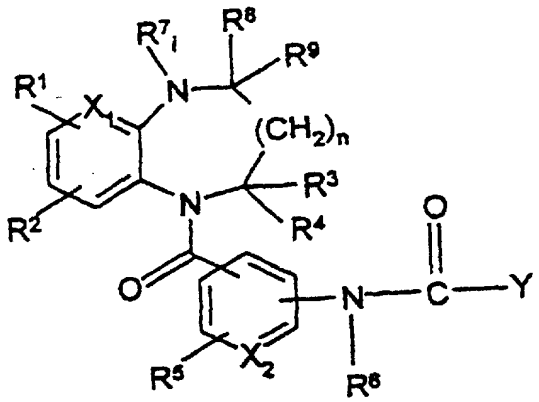


(I)

oder ihr Salz bereitzustellen, wobei in den obigen Formeln,

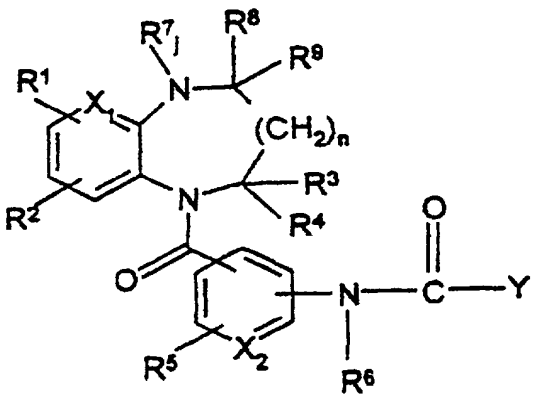
R^1, R^2, R^3, R^4, R^5, R^6, A, X_1, X_2, Y und n jeweils so wie oben definiert sind, oder

n) Unterwerfen einer Verbindung der Formel:



(It)

oder ihres Salzes unter einer Eliminierungsreaktion der Hydroxy-Schutzgruppe, um eine Verbindung der Formel:

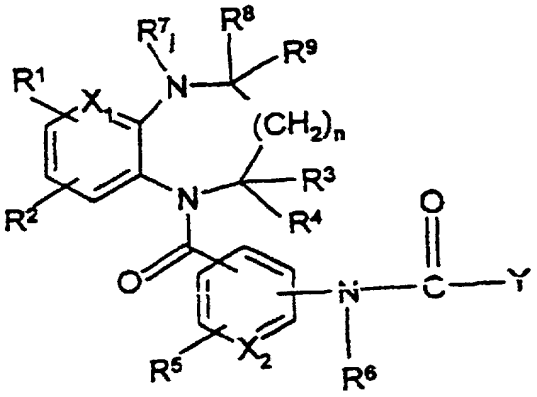


(Iu)

oder ihr Salz bereitzustellen, wobei in den obigen Formeln,

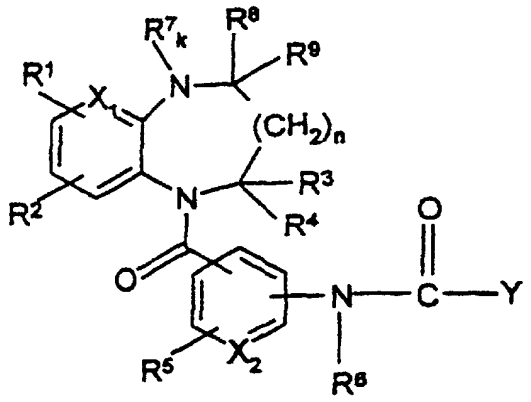
R^1, R^2, R^3, R^4, R^5, R^6, R^8, R^9, X_1, X_2, Y und n	jeweils so wie oben definiert sind,
R^7_i	ist ein (C_1-C_6) Alkyl, das substituiert ist mit (C_1-C_6) Alkoxy (C_1-C_6) alkoxy, (C_1-C_6) Alkoxy (C_1-C_6) alkoxy (C_1-C_6) alkoxy, Phenyl (C_1-C_6) alkoxy, Nitrophenyl (C_1-C_6) alkoxy, (C_1-C_6) Alkanoyloxy, Benzoyloxy, Fluorencarbonyloxy, (C_1-C_6) Alkoxycarbonyloxy, Phenyl (C_1-C_6)alkoxycarbonyloxy, Halogenphenyl (C_1-C_6) alkoxycarbonyloxy oder Tri (C_1-C_6)alkylsilyloxy, und
R^7_j	ist ein (C_1-C_6) Alkyl, das mit Hydroxy substituiert ist, oder

p) Reaktion einer Verbindung der Formel:



(Iu)

oder ihres Salzes mit einem Oxidationsmittel, um eine Verbindung der Formel :

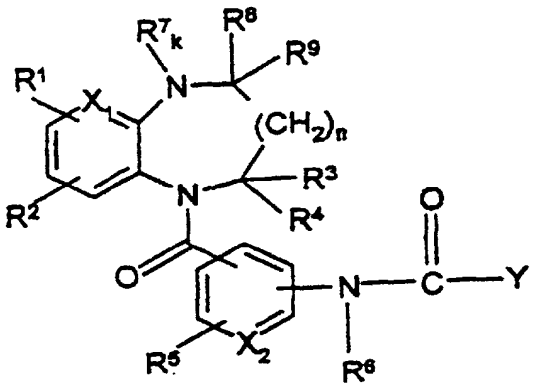


(Ix)

oder ihr Salz bereitzustellen, wobei in den obigen Formeln,

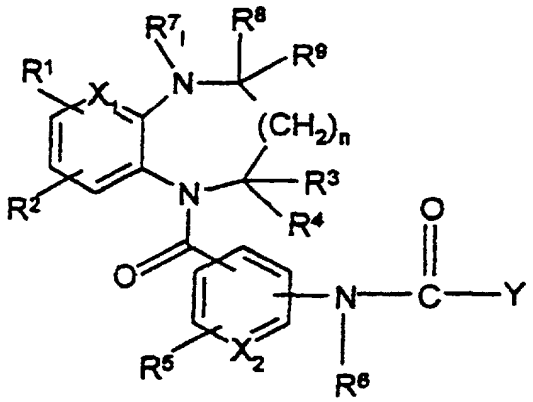
R^1, R^2, R^3, R^4, R^5, R^6, R^7_j, R^8, R^9, X_2, Y und n jeweils so wie oben definiert sind, und
R^7_k ist ein (C_1-C_6) Alkyl, das mit Formyl substituiert ist, oder

q) Reaktion einer Verbindung der Formel:



(Ix)

oder ihres Salzes mit Di (C_1-C_6) alkylamin, Piperidin oder N-(C_1-C_6) alkylpiperazin in Gegenwart eines Reduktionsmittels, um eine Verbindung der Formel :

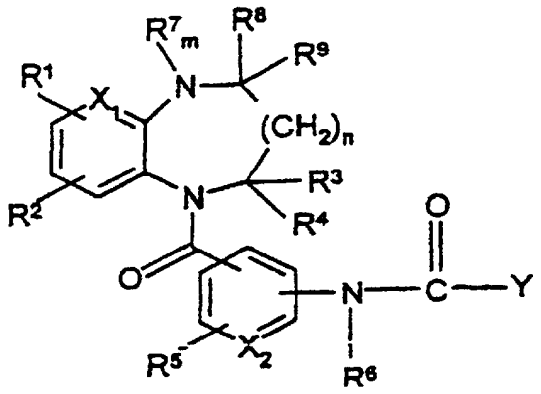


(Iy)

oder ihr Salz bereitzustellen, wobei in den obigen Formeln,

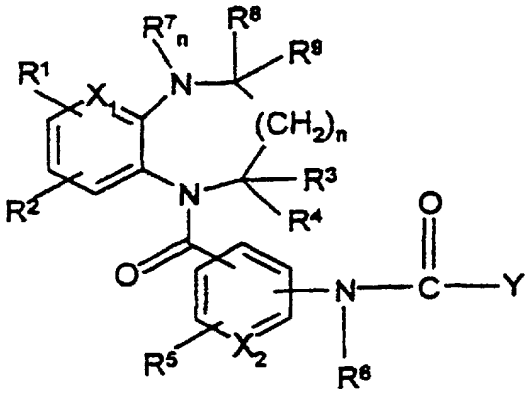
R^1, R^2, R^3, R^4, R^5, R^6, $R^7{}_k$, R^8, R^9, X_1, X_2, Y und n	jeweils so wie oben definiert sind, und
R_l	ist ein (C_1-C_6) Alkyl, das substituiert ist mit Di (C_1-C_6) alkylamino, Piperidyl oder N-(C_1-C_6)alkylpiperazinyl, oder

r) Unterwerfen einer Verbindung der Formel:



(Iz)

oder ihres Salzes unter eine Acylierungsreaktion, um eine Verbindung der Formel :

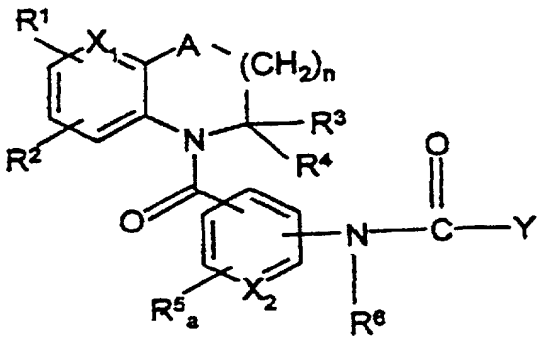


(I-1)

oder ihr Salz bereitzustellen, wobei in den obigen Formeln,

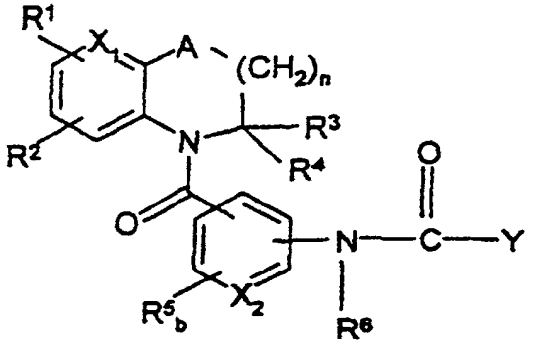
R^1, R^2, R^3, R^4, R^5, R^6, R^8, R^9, X_1, X_2, Y und n	jeweils so wie oben definiert sind,
$R^7{}_m$	ist ein (C_1-C_6) Alkyl, das substituiert ist mit N-[Hydroxy (C_1-C_6) alkyl]piperazinylcarbonyl, und
$R^7{}_n$	ist ein (C_1-C_6) Alkyl, das substituiert ist mit N-[(C_1-C_6) Alkanoyloxy (C_1-C_6) alkyl]piperazinylcarbonyl, oder

t) Reaktion einer Verbindung der Formel:



(I-4)

oder ihres Salzes mit (C_1-C_6) Alkylhalogenid oder ein Salz davon, (C_1-C_6) Alkyl, das mit (C_1-C_6) Alkylamino substituiert sein kann, in Gegenwart einer Base, um eine Verbindung der Formel :

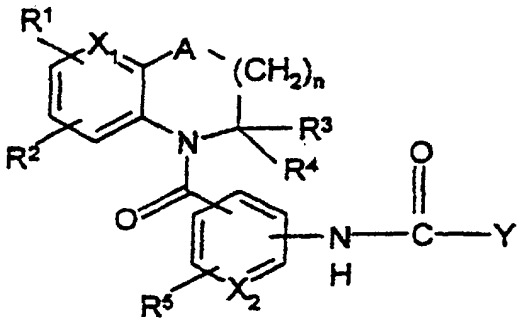


(I-5)

oder ihr Salz bereitzustellen, wobei in den obigen Formeln,

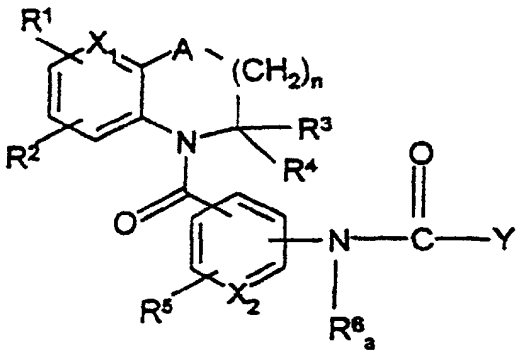
R^1, R^2, R^3, R^4, R^6, A, X_1, X_2, Y und n	jeweils so wie oben definiert sind,
$R^5{}_a$	Hydroxy ist, und
$R^5{}_b$	(C_1-C_6) Alkoxy ist, das optional substituiert ist mit (C_1-C_6) Alkylamino, oder

u) Reaktion einer Verbindung der Formel:



(Ia)

oder ihres Salzes mit einem Alkylierungsmittel oder einem Acylierungsmittel, um eine Verbindung der Formel :

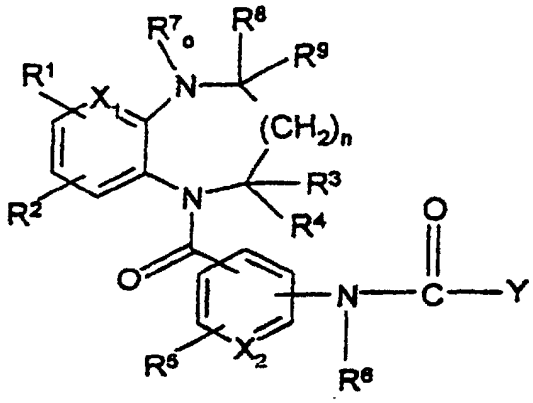


(I-6)

oder ihr Salz bereitzustellen, wobei in den obigen Formeln,

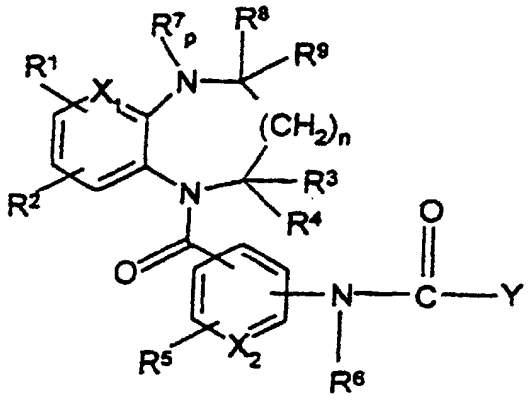
R^1, R^2, R^3, R^4, R^5, A, X_1, X_2, Y und n	jeweils so wie oben definiert sind, und
$R^6{}_a$	ist (C_1-C_6) Alkyl oder (C_1-C_6) Alkoxycarbonyl, oder

v) Reaktion einer Verbindung der Formel:



(I-7)

oder ihres Salzes mit (C_1-C_6) Alkylhalogenid, um eine Verbindung der Formel :



(I-8)

oder ihr Salz bereitzustellen, wobei in den obigen Formeln,

R^1, R^2, R^3, R^4, R^5, R^6, R^8, R^9, X_1, X_2, Y und n	jeweils so wie oben definiert sind,
$R^7{}_o$	ist ein (C_1-C_6) Alkyl, das substituiert ist mit N-(C_1-C_6) Alkylpiperazinylcarbonyl, und
$R^7{}_p$	ist ein (C_1-C_6) Alkyl, das substituiert ist mit N,N-di (C_1-C_6) alkyl)piperaziniocarbonyl.

8. Pharmazeutische Zusammensetzung, umfassend eine Verbindung nach Anspruch 1 als einen Wirkstoff in Assoziation mit einem pharmazeutisch akzeptablen, im Wesentlichen nicht-toxischen Trägerstoff oder Bindemittel.

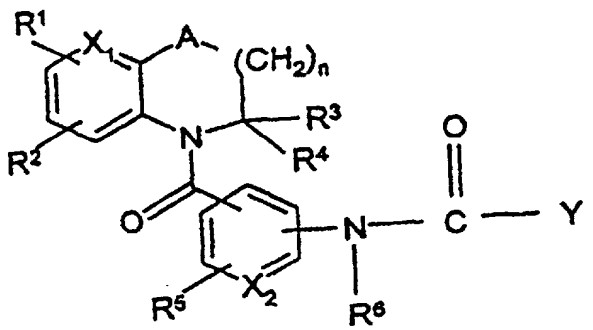
9. Verbindung nach Anspruch 1 für die Verwendung als Medikament.

10. Verbindung nach Anspruch 1 für die Verwendung bei der Behandlung und/oder Verhinderung von Hypertonie, Herzfehler, Niereninsuffizienz, Ödem, Aszites, Vasopressin-Parasekretionssyndrom, Leberzirrhose, Hyponatriämie, Hypokaliämie, Diabetes oder Kreislaufstörung.

11. Verwendung einer Verbindung nach Anspruch 1 für die Herstellung eines Medikamentes für die Behandlung und/oder Verhinderung von Hypertonie, Herzfehler, Niereninsuffizienz, Ödem, Aszites, Vasopressin-Parasekretionssyndrom, Leberzirrhose, Hyponatriämie, Hypokaliämie, Diabetes oder Kreislaufstörung beim Menschen oder bei Tieren.

Revendications

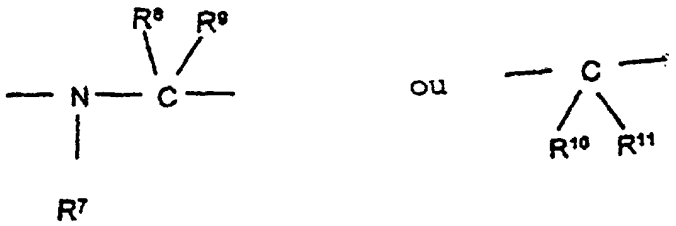
1. Composé de formule :



(I)

dans laquelle

R^1	est un hydrogène ou un alkyle en C_1-C_6,
R^2	est un hydrogène, un alkyle en C_1-C_6, un haloalkyle en C_1-C_6, un halogène ou un alcoxy en C_1-C_6,
R_3 et R_4	sont chacun un hydrogène, un alkyle en C_1-C_6, ou pris ensemble pour former un oxo,
R^5	est un hydrogène, un halogène, un nitro, un hydroxy, un alcoxy(en C_1-C_6)alcoxy en C_1-C_6, un alcoxy (en C_1-C_6)alcoxy(en C_1-C_6)alcoxy en C_1-C_6, un phénylalcoxy en C_1-C_6, un nitrophénylalcoxy en C_1-C_6, un alcanoyl(en C_1-C_6)oxy, un benzyloxy, un fluorènecarbonyloxy, un alcoxy(en C_1-C_6)carbonyloxy, un phénylalcoxy(en C_1-C_6)carbonyloxy, un halophénylalcoxy(en C_1-C_6)carbonyloxy, un trialkyl (en C_1-C_6)silyloxy, un alkyle en C_1-C_6 ou un alcoxy en C_1-C_6 éventuellement substitué avec un alkyl (en C_1-C_6) amino,
R^6	est un hydrogène, un alkyle en C_1-C_6 ou un alcoxy(en C_1-C_6)carbonyle,
A	est



dans lesquels

R^7 est un hydrogène; un alkyle en C_1-C_6 éventuellement substitué avec un halogène, un amino, un alkyl (en C_1-C_6)amino, un alcanoyl(en C_1-C_6)amino, un haloalcanoyl(en C_1-C_6)amino, un phtaloylamino, un alcoxy(en C_1-C_6)carbonylamino, un benzyloxycarbonylamino, un nitrobenzyloxycarbonylamino, un benzènesulfonylamino, un tosylamino, un nitrophénylsulfénylamino, un tritylamino, un benzylamino, un carboxy, un alcoxy(en C_1-C_6)carbonyle, un dialkyl(en C_1-C_6) aminoalcoxy(en C_1-C_6) carbonyle, un haloalcoxy(en C_1-C_6)carbonyle, un trihaloalcoxy(en C_1-C_6)carbonyle, un phénoxycarbonyle, un nitrophénoxycarbonyle, un naphtyloxycarbonyle, un phénylalcoxy(en C_1-C_6)carbonyle, un nitrophénylalcoxy(en C_1-C_6)carbonyle, un carbamoyle, un alkyl(en C_1-C_6)carbamoyle, un trihaloalcanoyle en C_1-C_6, un alcanoyle en C_1-C_6 non substitué, un toluoyle, un di(tert-butyl)benzoyle, un tolylbenzoyle, un aminobenzoyle, un tolylbenzoylaminobenzoyle, un benzoyle non substitué, un carbonyle hétérocylique contenant N, un alkyl(en C_1-C_6)sulfonyle, un tolylsulfonyle, un dialcoxy(en C_1-C_6)phénylsulfonyle, un phénylsulfonyle non-substitué, un pipéridyle, un pyridyle, un N-alkyl(en C_1-C_6)pipérazinyle, un hydroxy, un alcoxy(en C_1-C_6)alcoxy en C_1-C_6, un alcoxy(en C_1-C_6)alcoxy(en C_1-C_6)alcoxy en C_1-C_6, un phénylalcoxy en C_1-C_6, un nitrophénylalcoxy en C_1-C_6, un alcanoyl (en C_1-C_6)oxy, un benzoyloxy, un fluorènecarbonyloxy, un alcoxy(en C_1-C_6)carbonyloxy, un phénylalcoxy (en C_1-C_6)carbonyloxy, un halophénylalcoxy(en C_1-C_6)carbonyloxy, un trialkyl(en C_1-C_6)silyloxy ou un diméthoxyphénylsulfonyle; et

R^8 et R^9 sont pris ensemble pour former un oxo ou un thioxo;

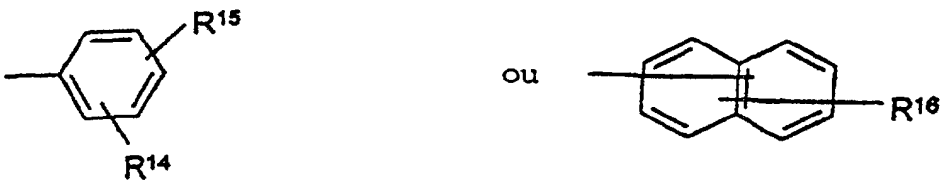
R^{10} est un hydrogène;

R^{11} est un hydrogène, ou un alkyl(en C_1-C_6)amino;

X_1 est CH,

X_2 est CH ou N,

Y est



dans lesquels

R^{14} est un hydrogène, un halogène, un hydroxy ou un alcoxy en C_1-C_6,

R^{15} est un phénoxy, un naphtyle, un phényle substitué avec un ou des substituants choisis dans le groupe constitué par un alkyle en C_1-C_6, un alcoxy en C_1-C_6, un halogène, un haloalkyle en C_1-C_6, un hydroxy, un aminoalkyle en C_1-C_6, un azidoalkyle en C_1-C_6, un alkyl(en C_1-C_6)aminoalkyle en C_1-C_6, un alcanoyl (en C_1-C_6)aminoalkyle en C_1-C_6, un hydroxyalkyle en C_1-C_6, un cyano, un carboxy, un alcoxy(en C_1-C_6) carbonyle, un dialkyl(en C_1-C_6)aminoalcoxy(en C_1-C_6)carbonyle, un haloalcoxy(en C_1-C_6)carbonyle, un trihaloalcoxy(en C_1-C_6)carbonyle, un phénoxycarbonyle, un nitrophénoxycarbonyle, un naphtyloxycarbonyle, un phénylalcoxy(en C_1-C_6)carbonyle, un nitrophénylalcoxy(en C_1-C_6)carbonyle, un pyridyle ou un pyrrolyle, et

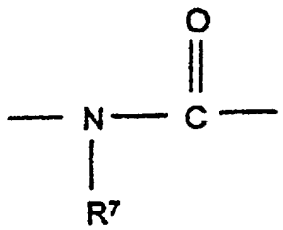
R^{16} est un tolyle et

n est 0, 1, 2 ou 3,

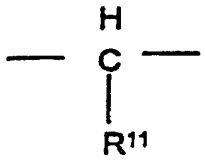
et des sels pharmaceutiquement acceptables de celui-ci.

2. Composé selon la revendication 1, dans lequel

R^1 est un hydrogène,
R^2 est un hydrogène, un alkyle en C_1-C_6, ou un halogène,
R^3 est un hydrogène,
R^4 est un hydrogène,
R^5 est un hydrogène ou un alcoxy en C_1-C_6,
R^6 est un hydrogène,
A est

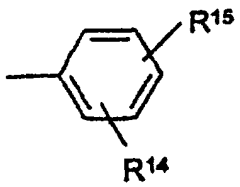


ou



dans lesquels

R^7 est un hydrogène; ou un alkyle en C_1-C_6 éventuellement substitué avec un amino, un alkyl(en C_1-C_6)amino, un alcanoyl(en C_1-C_6)amino, un haloalcanoyl(en C_1-C_6)amino, un phtaloylamino, un alcoxy(en C_1-C_6)carbonylamino, un benzyloxycarbonylamino, un nitrobenzyloxycarbonylamino, un benzènesulfonylamino, un tosylamino, un nitrophénylsulfénylamino, un tritylamino, un benzylamino, un carboxy, un alcoxy(en C_1-C_6) carbonyle, un dialkyl(en C_1-C_6) aminoalcoxy (en C_1-C_6) carbonyle, un haloalcoxy(en C_1-C_6)carbonyle, un trihaloalcoxy(en C_1-C_6)carbonyle, un phénoxycarbonyle, un nitrophénoxycarbonyle, un naphtyloxycarbonyle, un phénylalcoxy(en C_1-C_6) carbonyle, un nitrophénylalcoxy(en C_1-C_6) carbonyle, un carbamoyle, un alkyl(en C_1-C_6) carbamoyle, un trihaloalcanoyle en C_1-C_6, un alcanoyle en C_1-C_6 non substitué, un toluoyle, un di(tert-butyl)benzoyle, un tolylbenzole, un aminobenzoyle, un tolylbenzoylaminobenzoyle, un benzoyle non substitué, un carbonyle hétérocylique contenant N, un alkyl(en C_1-C_6)sulfonyle, un tolylsulfonyle, un dialcoxy(en C_1-C_6)phénylsulfonyle, un phénylsulfonyle non-substitué, un pipéridyle, un pyridyle, un N-alkyl (en C_1-C_6)pipérazinyle; et
R^{11} est un hydrogène ou un alkyl(en C_1-C_6)amino,
X_1 est CH,
X_2 est CH,
Y est



dans lequel

R^{14} et R^{15} sont chacun tels que définis ci-dessus, et
n est 0, 1 ou 2.

3. Composé selon la revendication 2, dans lequel

A est

dans lesquels

R^7 est alkyle inférieur éventuellement substitué avec un amino, un alkyl(en C_1-C_6)amino, un alcanoyl(en C_1-C_6)amino, un haloalcanoyl(en C_1-C_6)amino, un phtaloylamino, un alcoxy(en C_1-C_6)carbonylamino, un benzyloxycarbonylamino, un nitrobenzyloxycarbonylamino, un benzènesulfonylamino, un tosylamino, un nitrophénylsulfénylamino, un tritylamino, un benzylamino, un carboxy, un alcoxy(en C_1-C_6)carbonyle, un dialkyl(en C_1-C_6)aminoalcoxy(en C_1-C_6)carbonyle, un haloalcoxy(en C_1-C_6)carbonyle, un trihaloalcoxy(en C_1-C_6)carbonyle, un phénoxycarbonyle, un nitrophénoxycarbonyle, un naphtyloxycarbonyle, un phénylalcoxy(en C_1-C_6)carbonyle, un nitrophénylalcoxy(en C_1-C_6)carbonyle, un carbamoyle, un alkyl(en C_1-C_6)carbamoyle, un trihaloalcanoyle en C_1-C_6, un alcanoyle en C_1-C_6 non substitué, un toluoyle, un di(tert-butyl)benzoyle, un tolylbenzoyle, un aminobenzoyle, un tolylbenzoylaminobenzoyle, un benzoyle non substitué, un carbonyle hétérocylique contenant N, un alkyl(en C_1-C_6) sulfonyle, un tolylsulfonyle, un dialcoxy(en C_1-C_6)phénylsulfonyle, un phénylsulfonyle non-substitué ou un pipéridino; et

R^{11} est un hydrogène ou un alkyl(en C_1-C_6)amino, et

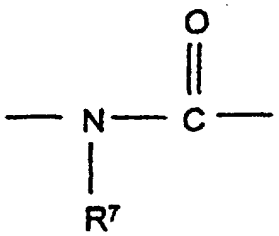
Y est

dans lequel

R^{15} est un phényle substitué avec un ou des substituants choisis dans le groupe constitué par un alkyle en C_1-C_6, un alcoxy en C_1-C_6, un halogène, un haloalkyle en C_1-C_6, un hydroxy, un aminoalkyle en C_1-C_6, un azidoalkyle en C_1-C_6, un alkyl(en C_1-C_6)aminoalkyle en C_1-C_6, un alcanoyl(en C_1-C_6)aminoalkyle en C_1-C_6, un hydroxyalkyle en C_1-C_6, un cyano, un carboxy, un alcoxy(en C_1-C_6)carbonyle, un dialkyl(en C_1-C_6)aminoalcoxy(en C_1-C_6)carbonyle, un haloalcoxy(en C_1-C_6)carbonyle, un trihaloalcoxy(en C_1-C_6)carbonyle, un phénoxycarbonyle, un nitrophénoxycarbonyle, un naphtyloxycarbonyle, un phénylalcoxy(en C_1-C_6)carbonyle et un nitrophénylalcoxy(en C_1-C_6)carbonyle.

4. Composé selon la revendication 3, dans lequel

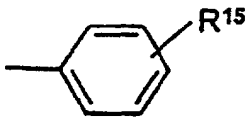
A est



dans lequel

R^7 est alkyle en C_1-C_6 substitué avec un N-alkyl(en C_1-C_6)pipérazinylcarbonyle ou un alkyle en C_1-C_6 substitué avec un dialkyl(en C_1-C_6)amino, et

Y est

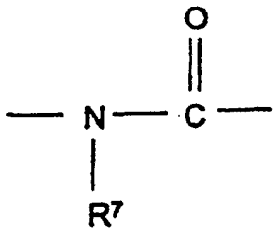


dans lequel

R^{15} est un phényle substitué avec un alkyle en C_1-C_6 ou un dialkyle en C_1-C_6.

5. Composé selon la revendication 4,
dans lequel

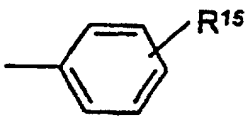
R^2 est un hydrogène,
R^5 est un hydrogène,
A est



dans lequel

R^7 est alkyle en C_1-C_6 substitué avec un N-alkyl(en C_1-C_6)pipérazinylcarbonyle,

Y est



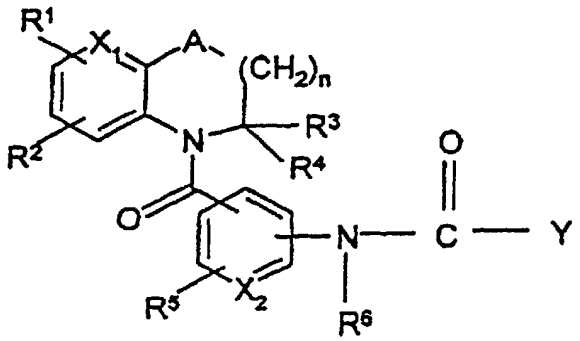
dans lequel

R^{15} est un phényle substitué avec un alkyle en C_1-C_6 ou un dialkyle en C_1-C_6 et

n est 1.

6. Composé selon la revendication 5, qui est le 5-{4-[2-(4-méthylphényl)benzoylamino]benzoyl}-1-[(4-méthyl-1-pipérazinyl)carbonylméthyl]-1,3,4,5-tétrahydro-1,5-benzodiazépin-2(2H)-one.

7. Procédé pour la préparation d'un composé de formule



(I)

dans laquelle

R^1 est un hydrogène ou un alkyle en C_1-C_6,
R^2 est un hydrogène, un alkyle en C_1-C_6, un haloalkyle en C_1-C_6, un halogène ou un alcoxy en C_1-C_6,
R^3 et R^4 sont chacun un hydrogène, un alkyle en C_1-C_6, ou pris ensemble pour former un oxo,
R^5 est un hydrogène, un halogène, un nitro, un hydroxy, un alcoxy(en C_1-C_6)alcoxy en C_1-C_6, un alcoxy(en C_1-C_6)alcoxy(en C_1-C_6)alcoxy en C_1-C_6, un phénylalcoxy en C_1-C_6, un nitrophénylalcoxy en C_1-C_6, un alcanoyl(en C_1-C_6)oxy, un benzyloxy, un fluorènecarbonyloxy, un alcoxy(en C_1-C_6)carbonyloxy, un phénylalcoxy(en C_1-C_6)carbonyloxy, un halophénylalcoxy(en C_1-C_6)carbonyloxy, un trialkyl(en C_1-C_6)silyloxy, un alkyle en C_1-C_6 ou un alcoxy en C_1-C_6 éventuellement substitué avec un alkyl(en C_1-C_6)amino,
R^6 est un hydrogène, un alkyle en C_1-C_6 ou un alcoxy(en C_1-C_6)carbonyle,
A est

dans lesquels

R^7 est un hydrogène; un alkyle en C_1-C_6 éventuellement substitué avec un halogène, un amino, un alkyl (en C_1-C_6)amino, un alcanoyl(en C_1-C_6)amino, un haloalcanoyl(en C_1-C_6)amino, un phtaloylamino, un alcoxy(en C_1-C_6)carbonylamino, un benzyloxycarbonylamino, un nitrobenzyloxycarbonylamino, un benzènesulfonylamino, un tosylamino, un nitrophénylsulfénylamino, un tritylamino, un benzylamino, un carboxy, un alcoxy(en C_1-C_6)carbonyle, un dialkyl (en C_1-C_6)aminoalcoxy(en C_1-C_6) carbonyle, un haloalcoxy(en C_1-C_6)carbonyle, un trihaloalcoxy(en C_1-C_6)carbonyle, un phénoxycarbonyle, un nitrophénoxycarbonyle, un naphtyloxycarbonyle, un phénylalcoxy(en C_1-C_6)carbonyle, un nitrophénylalcoxy(en C_1-C_6)carbonyle, un carbamoyle, un alkyl (en C_1-C_6)carbamoyle, un trihaloalcanoyle en C_1-C_6, un alcanoyle en C_1-C_6 non substitué, un toluoyle, un di(tert-butyl)benzoyle, un tolylbenzoyle, un aminobenzoyle, un tolylbenzoylaminobenzoyle, un benzoyle non substitué, un carbonyle hétéro-

cylique contenant N, un alkyl(en C_1-C_6)sulfonyle, un tolylsulfonyle, un dialcoxy(en C_1-C_6)phénylsulfonyle, un phénylsulfonyle non-substitué, un pipéridyle, un pyridyle, un N-alkyl(en C_1-C_6)pipérazinyle, un hydroxy, un alcoxy(en C_1-C_6)alcoxy en C_1-C_6, un alcoxy(en C_1-C_6)alcoxy(en C_1-C_6)alcoxy en C_1-C_6, un phénylalcoxy en C_1-C_6, un nitrophénylalcoxy en C_1-C_6, un alcanoyl(en C_1-C_6)oxy, un benzoyloxy, un fluorènecarbonyloxy, un alcoxy(en C_1-C_6)carbonyloxy, un phénylalcoxy(en C_1-C_6)carbonyloxy, un halophénylalcoxy(en C_1-C_6)carbonyloxy, un trialkyl(en C_1-C_6)silyloxy ou un diméthoxyphénylsulfonyle; et

R^8 et R^9 sont pris ensemble pour former un oxo ou un thioxo; ou

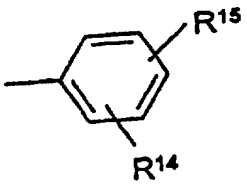
R^{10} est un hydrogène;

R^{11} est un hydrogène, ou un alkyl(en C_1-C_6)amino;

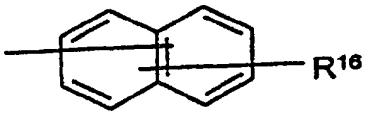
X_1 est CH,

X_2 est CH ou N,

Y est



ou



dans lesquels

R^{14} est un hydrogène, un halogène, un hydroxy ou un alcoxy en C_1-C_6,

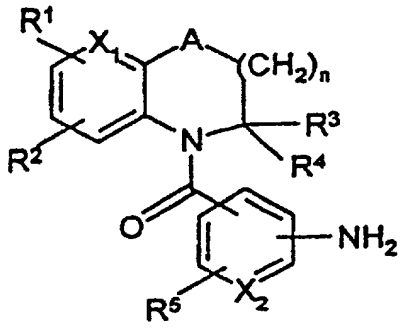
R^{15} est un phénoxy, un naphtyle, un phényle substitué avec un ou des substituants choisis dans le groupe constitué par un alkyle en C_1-C_6, un alcoxy en C_1-C_6, un halogène, un haloalkyle en C_1-C_6, un hydroxy, un aminoalkyle en C_1-C_6, un azidoalkyle en C_1-C_6, un alkyl(en C_1-C_6)aminoalkyle en C_1-C_6, un alcanoyl (en C_1-C_6)aminoalkyle en C_1-C_6, un hydroxyalkyle en C_1-C_6, un cyano, un carboxy, un alcoxy(en C_1-C_6) carbonyle, un dialkyl (en C_1-C_6)aminoalcoxy(en C_1-C_6)carbonyle, un haloalcoxy(en C_1-C_6)carbonyle, un trihaloalcoxy(en C_1-C_6)carbonyle, un phénoxycarbonyle, un nitrophénoxycarbonyle, un naphtyloxycarbonyle, un phénylalcoxy(en C_1-C_6) carbonyle, un nitrophénylalcoxy(en C_1-C_6)carbonyle, un pyridyle ou un pyrrolyle, et

R^{16} est un tolyle et

n est 0, 1, 2 ou 3,

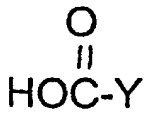
ou des sels de celui-ci, qui comprend le fait de

a) faire réagir un composé de formule



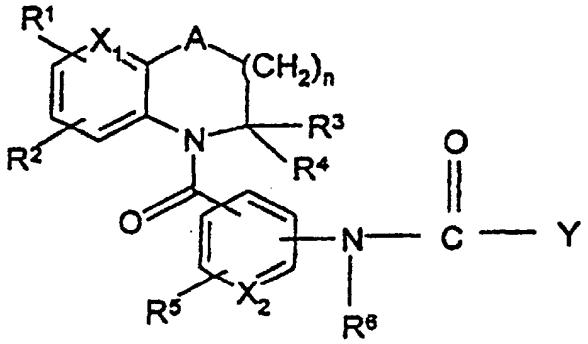
(II)

ou son sel avec un composé de formule :



(III)

ou son dérivé réactif au groupe carboxy ou un sel de celui-ci pour fournir un composé de formule :

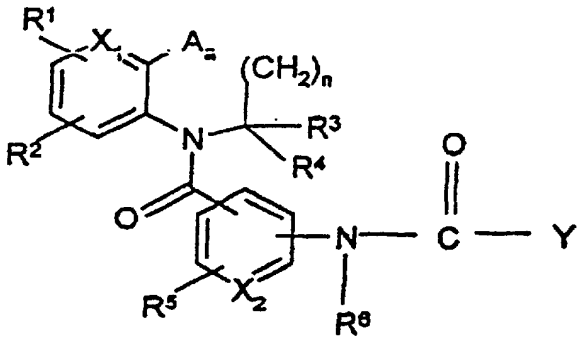


(Ia)

ou son sel,
dans les formules ci-dessus,

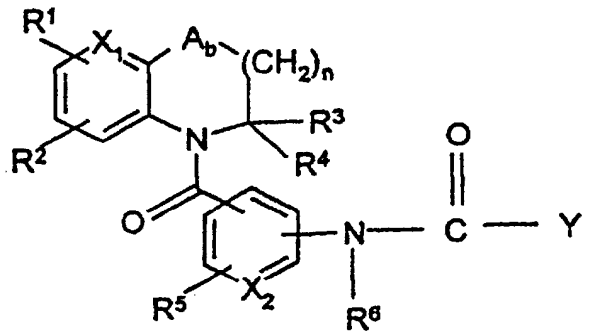
R^1, R^2, R^3, R^4, R^5, A, X_1, X_2, Y et n sont chacun tels que définis ci-dessus, ou

b) faire réagir un composé de formule :



(Ib)

ou son dérivé réactif au groupe carboxy ou un sel de celui-ci avec une amine pour fournir un composé de formule

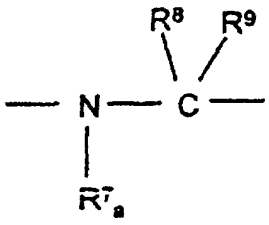


(Ic)

ou son sel,
dans les formules ci-dessus,

R^1, R^2, R^3, R^4, R^5, R^6, X_1, X_2, Y et n sont chacun tels que définis ci-dessus,

A_a est

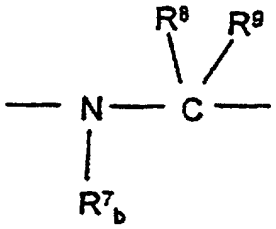


dans lequel

R^8 et R^9 sont chacun tels que définis ci-dessus;

$R^7{}_a$ est un alkyle en C_1-C_6 substitué avec un carboxy, et

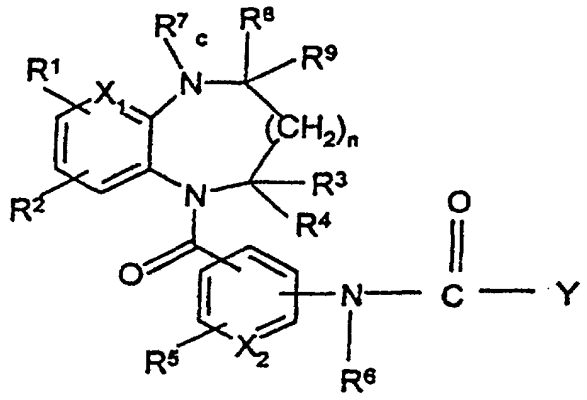
A_b est



dans lequel

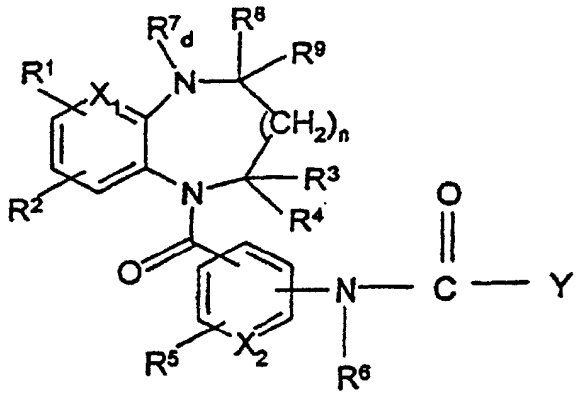
R^8 et R^9 sont chacun tels que définis ci-dessus;
$R^7{}_b$ est un alkyle en C_1-C_6 substitué avec un carbamoyle qui peut être substitué avec un.alkyle en C_1-C_6, ou un carbonyle hétérocyclique contenant N; ou

c) soumettre un composé de formule



(Id)

ou son sel à une réaction d'élimination du groupe protecteur de N pour fournir un composé de formule :

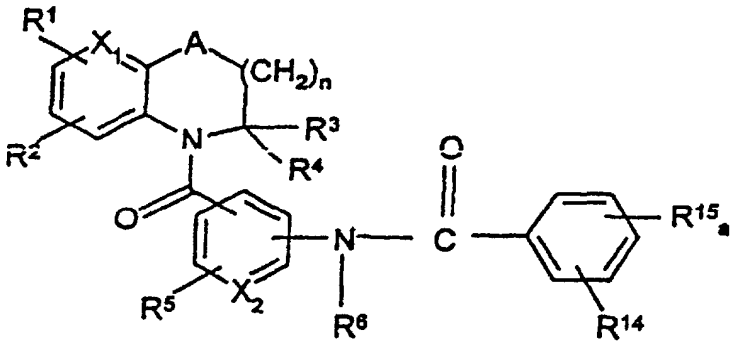


(Ie)

ou son sel,
dans les formules ci-dessus,

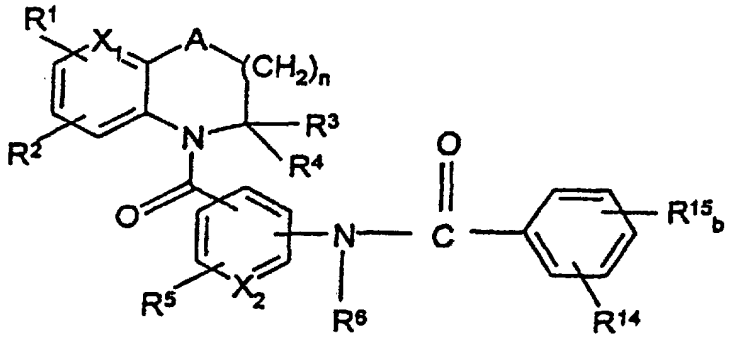
R^1, R^2, R^3, R^4, R^5, R^6, R^8, R^9, X_1, X_2, Y et n	sont chacun tels que définis ci-dessus,
$R^7{}_c$	est un alkyle en C_1-C_6 substitué avec un alcanoyl(en C_1-C_6) amino, un haloalcanoyl(en C_1-C_6)amino, un phtaloylamino, un alcoxy(en C_1-C_6)carbonylamino, un benzyloxycarbonylamino, un nitrobenzyloxycarbonylamino, un benzènesulfonylamino, un tosylamino, un nitrophénylsulfénylamino, un tritylamino, un benzylamino ou un N-alcoxy(en C_1-C_6)carbonylpipérazinylcarbonyle, et
$R^7{}_d$	est un alkyle en C_1-C_6 substitué avec un amino ou un pipérazinylcarbonyle, ou

d) soumettre un composé de formule :



(If)

ou son sel à une réduction pour fournir un composé de formule :

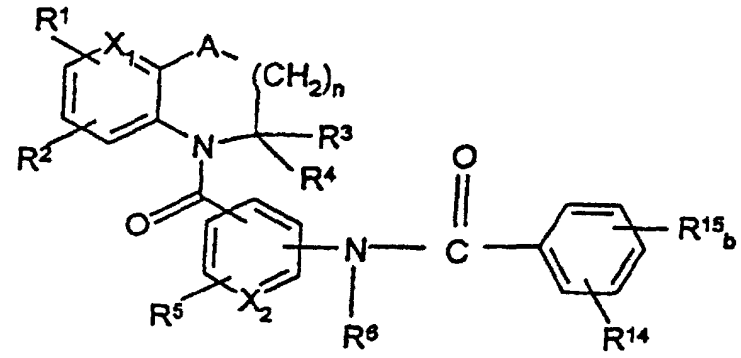


(Ig)

ou son sel,
dans les formules ci-dessus,

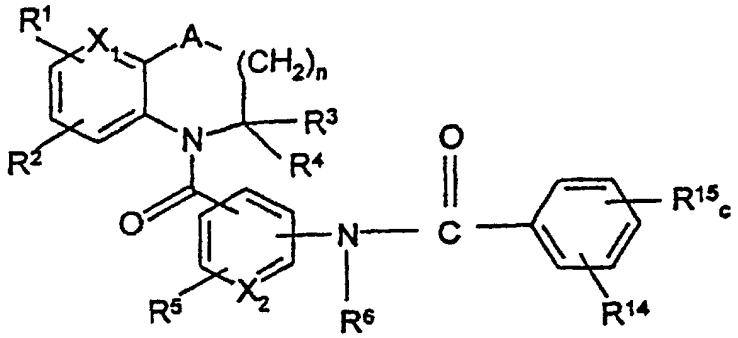
R^1, R^2, R^3, R^4, R^5, R^6, R^{14}, A, X_1, X_2, Y et n	sont chacun tels que définis ci-dessus,
$R^{15}{}_a$	est un phényle substitué avec un azidoalkyle en C_1-C_6, et
$R^{15}{}_b$	est un phényle substitué avec un aminoalkyle en C_1-C_6, ou

e) faire réagir un composé de formule :



(Ig)

ou son sel avec un agent acylant pour fournir un composé de formule :



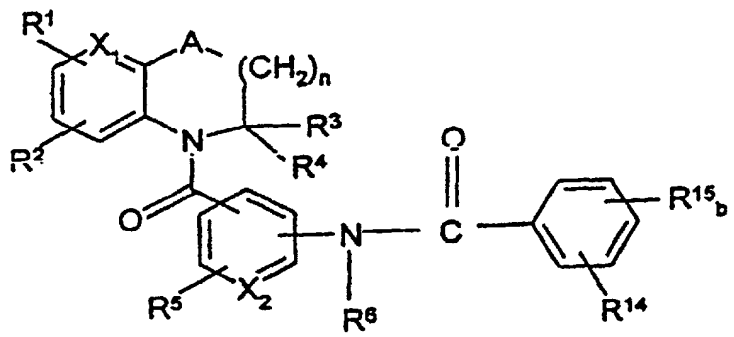
(Ih)

ou son sel,

dans les formules ci-dessus, R^1, R^2, R^3, R^4, R^5, R^6, R^{14}, $R^{15}{}_b$, A, X_1, X_2 et n sont chacun tels que définis ci-dessus, et

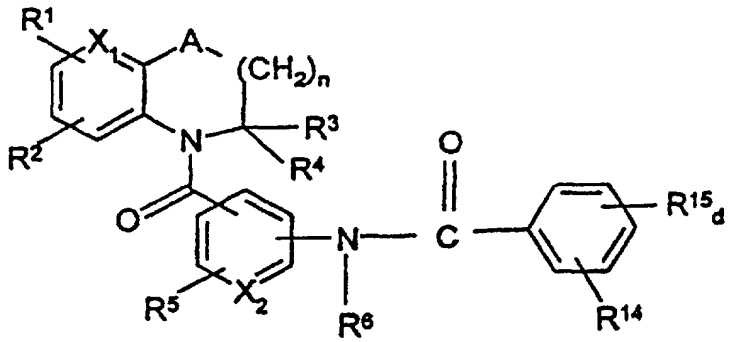
$R^{15}{}_c$ est un phényle substitué avec un alcanoyl(en C_1-C_6)aminoalkyle en C_1-C_6,

f) faire réagir un composé de formule :



(Ig)

ou son sel avec un agent alkylant pour fournir un composé de formule :



(Ii)

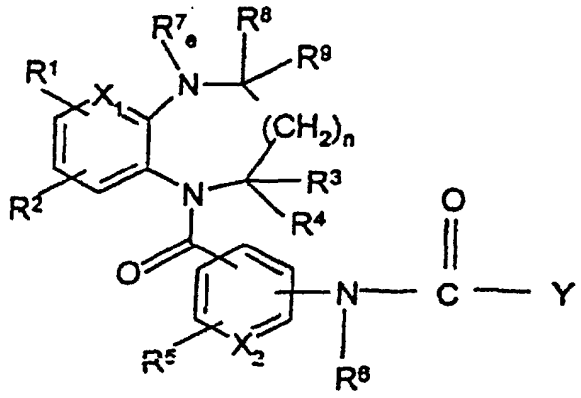
ou son sel,

dans les formules ci-dessus,

R^1, R^2, R^3, R^4, R^5, R^6, R^{14}, $R^{15}{}_b$, A, X_1, X_2 et n sont chacun tels que définis ci-dessus, et

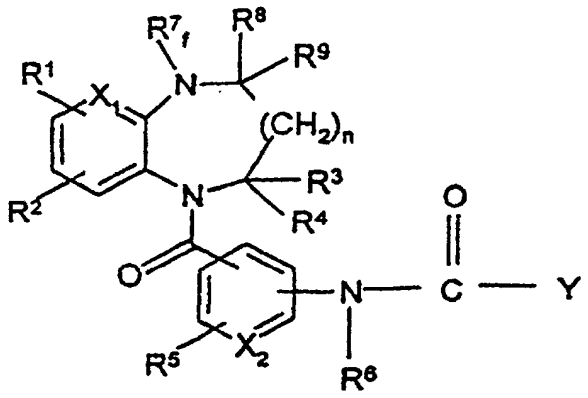
$R^{15}{}_d$ est un phényle substitué avec un alkyl(en C_1-C_6)aminoalkyle en C_1-C_6, ou

g) faire réagir un composé de formule :



(Ij)

ou son sel avec un agent alkylant pour fournir un composé de formule :

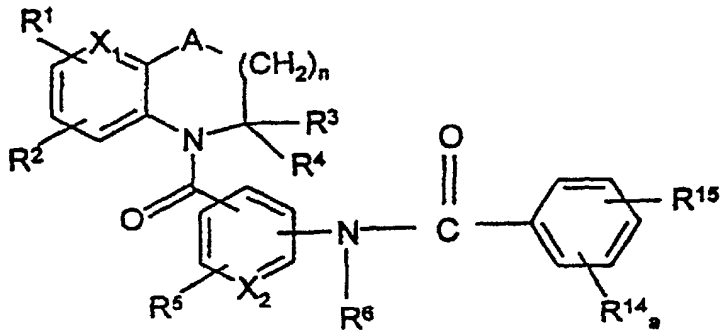


(Ik)

ou son sel,
dans les formules ci-dessus,

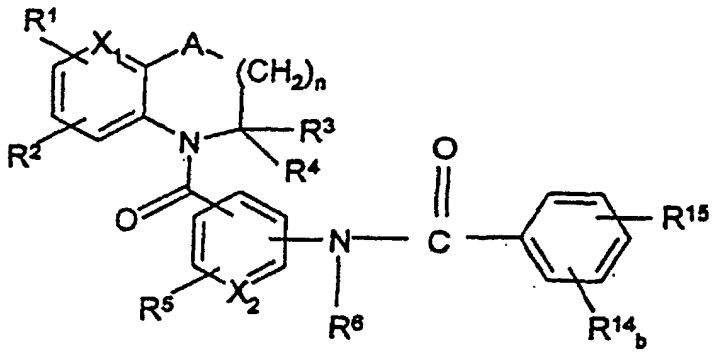
R^1, R^2, R^3, R^4, R^5, R^6, R^8, R^9, X_1, X_2, Y et n sont chacun tels que définis ci-dessus, et
$R^7{}_e$ est un alkyle en C_1-C_6 substitué avec un amino, et
$R^7{}_f$ est un alkyle en C_1-C_6 substitué avec un alkyl(en C_1-C_6)amino, ou

h) soumettre un composé de formule :



(Il)

ou son sel à une réaction de désalkylation pour fournir un composé de formule :

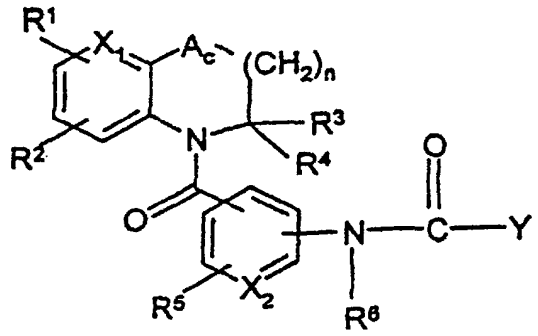


(Im)

ou son sel,
dans les formules ci-dessus,

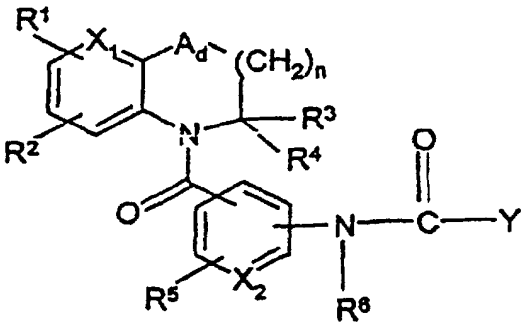
R^1, R^2, R^3, R^4, R^5, R^6, R^{15}, A, X_1, X_2 et n	sont chacun tels que définis ci-dessus, et
$R^{14}{}_a$	est un alcoxy en C_1-C_6, et
$R^{14}{}_b$	est un hydroxy, ou

i) soumettre un composé de formule :



(In)

ou son sel à une réaction de désestérification pour fournir un composé de formule :

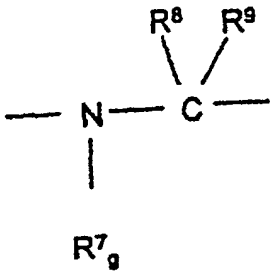


(Io)

ou son sel,
dans les formules ci-dessus,

R^1, R^2, R^3, R^4, R^5, R^6, X_1, X_2, Y et n sont chacun tels que définis ci-dessus,

A_c est

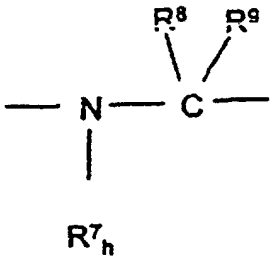


dans lequel

R^8 et R^9 sont chacun tels que définis ci-dessus; et

$R^7{}_g$ est un alkyle en C_1-C_6 substitué avec un alcoxy(en C_1-C_6)carbonyle, un dialkyl (en C_1-C_6) aminoalcoxy(en C_1-C_6) carbonyle, un haloalcoxy(en C_1-C_6)carbonyle, un trihaloalcoxy(en C_1-C_6)carbonyle, un phénoxycarbonyle, un nitrophénoxycarbonyle, un naphtyloxycarbonyle, un phénylalcoxy(en C_1-C_6)carbonyle, un nitrophénylalcoxy(en C_1-C_6)carbonyle ou un N-[alcoxy(en C_1-C_6) carbonylalkyl (en C_1-C_6)]-pipérazinylcarbonyle; et

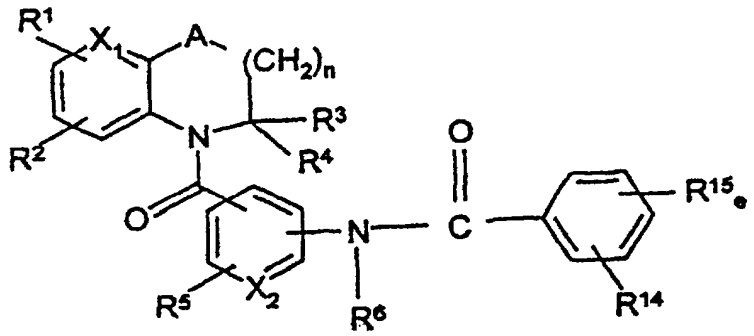
A_d est



dans lequel

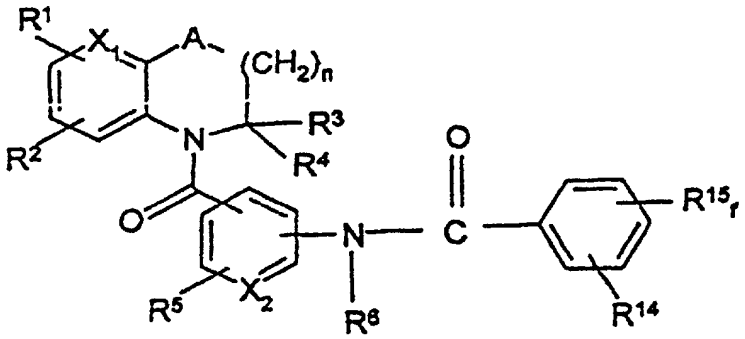
R^8 et R^9 sont chacun tels que définis ci-dessus; et
$R^7{}_h$ est un alkyle en C_1-C_6 substitué avec un carboxy ou un N- [carboxyalkyl (en C_1-C_6)]pipérazinyl-carbonyle, ou

f) faire réagir un composé de formule :



(Ip)

ou son dérivé réactif au groupe carboxy ou un sel de celui-ci avec un composé hydroxy pour fournir un composé de formule :

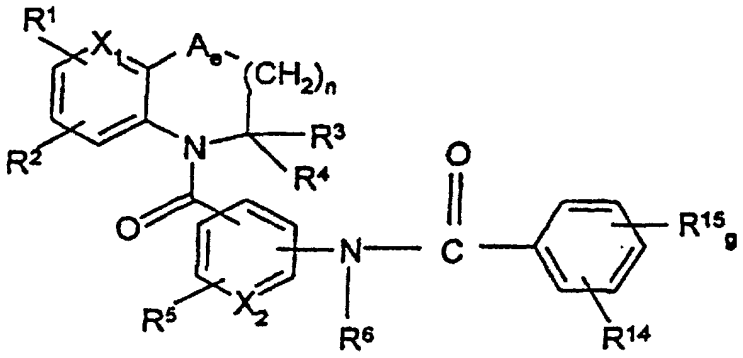


(Iq)

ou son sel,
dans les formules ci-dessus,

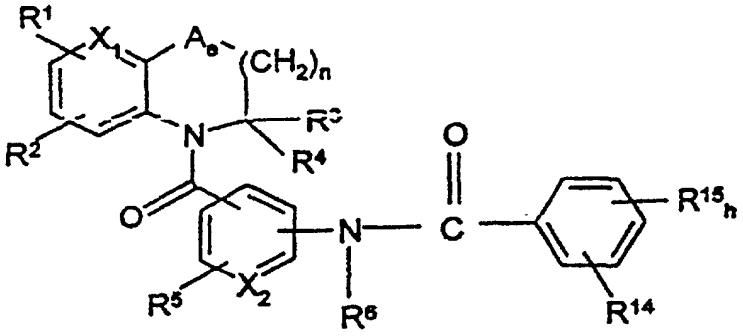
R^1, R^2, R^3, R^4, R^5, R^6, R^{14}, A, X_1, X_2 et n sont chacun tels que définis ci-dessus,
$R^{15}{}_e$ est un phényle substitué avec un carboxy, et
$R^{15}{}_f$ est un phényle substitué avec un alcoxy(en C_1-C_6)carbonyle, un dialkyl (en C_1-C_6)aminoalcoxy(en C_1-C_6)carbonyle, un haloalcoxy(en C_1-C_6)carbonyle, un trihaloalcoxy(en C_1-C_6)carbonyle, un phénoxycarbonyle, un nitrophénoxycarbonyle, un naphtyloxycarbonyle, un phénylalcoxy(en C_1-C_6)carbonyle ou un nitrophénylalcoxy(en C_1-C_6) carbonyle, ou

k) faire réagir un composé de formule :



(Ir)

ou son sel avec un agent réducteur pour fournir un composé de formule :

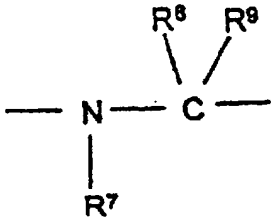


(Is)

ou son sel,
dans les formules ci-dessus,

R^1, R^2, R^3, R^4, R^5, R^6, R^{14}, X_1, X_2 et n sont chacun tels que définis ci-dessus,

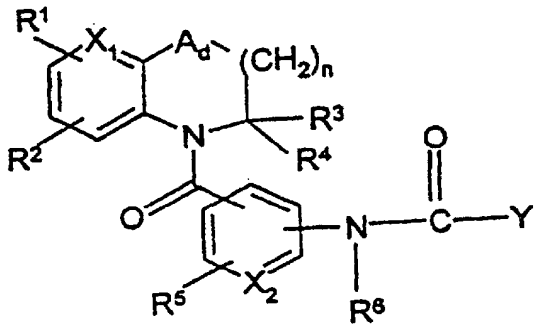
A_e est



dans lequel

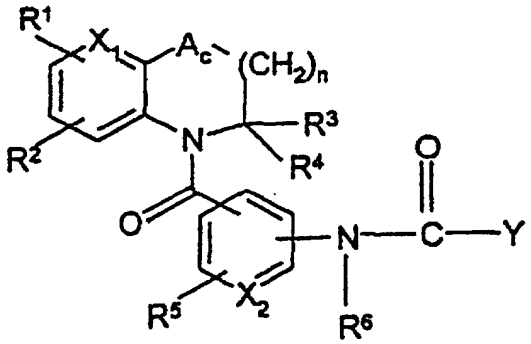
R^7, R^8 et R^9 sont chacun tels que définis ci-dessus,
$R^{15}{}_g$ est un phényle substitué avec un carboxy ou un alcoxy(en C_1-C_6)carbonyle, et
$R^{15}{}_h$ est un phényle substitué avec un hydroxyméthyle, ou

l) faire réagir un composé de formule :



(Io)

ou son dérivé réactif au groupe carboxy ou un sel de celui-ci avec un composé hydroxy pour fournir un composé de formule :

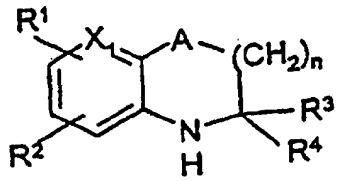


(In)

ou son sel,
dans les formules ci-dessus,

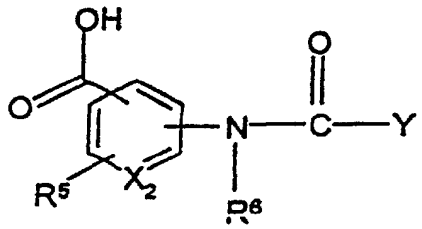
R^1, R^2, R^3, R^4, R^5, R^6, A_c, A_d, X_1, X_2, Y et n sont chacun tels que définis ci-dessus, ou

m) faire réagir un composé de formule :



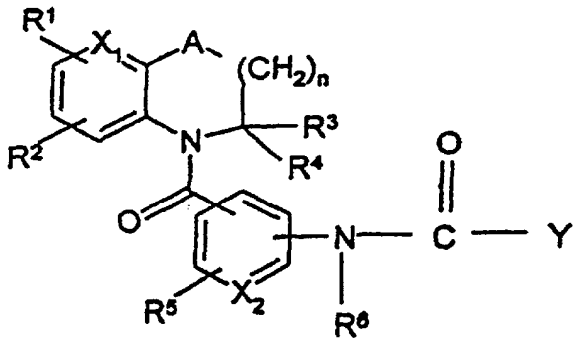
(IV)

ou son sel avec un composé de formule :



(V)

ou son dérivé réactif au groupe carboxy ou un sel de celui-ci pour fournir un composé de formule :

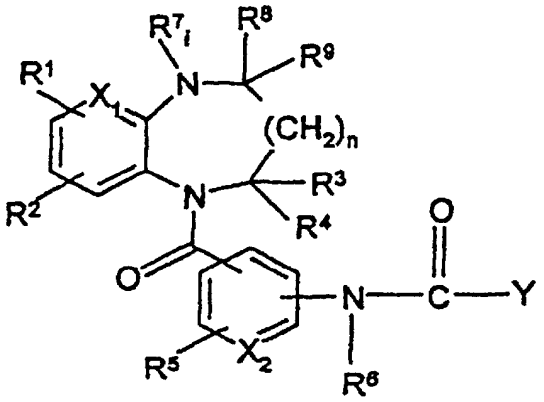


(I)

ou son sel,
dans les formules ci-dessus,

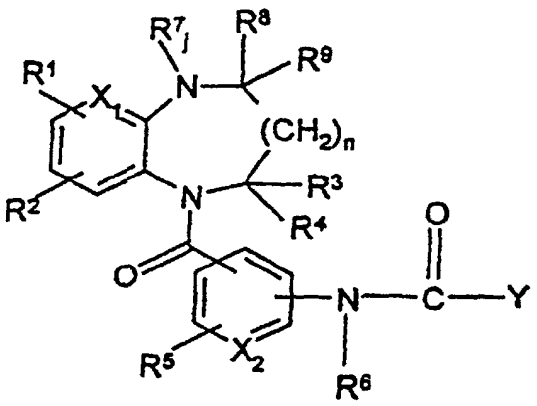
R^1, R^2, R^3, R^4, R^5, R^6, A, X_1, X_2, Y et n sont chacun tels que définis ci-dessus, ou

n) soumettre un composé de formule :



(It)

ou son sel,
à une réaction d'élimination du groupe protecteur de l'hydroxy pour fournir un composé de formule :



(Iu)

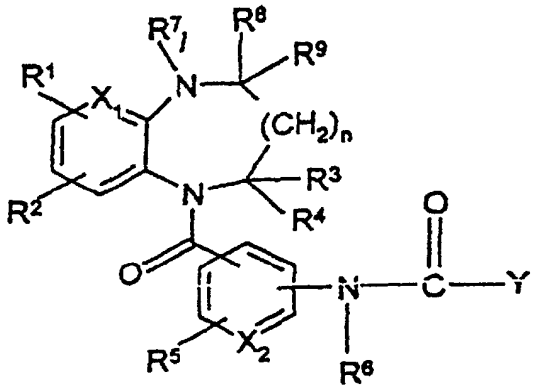
ou son sel,
dans les formules ci-dessus,

R^1, R^2, R^3, R^4, R^5, R^6, R^8, R^9, X_1, X_2, Y et n sont chacun tels que définis ci-dessus,

R^7_i est un alkyle en C_1-C_6 substitué avec un alcoxy(en C_1-C_6) alcoxy en C_1-C_6, un alcoxy(en C_1-C_6)alcoxy(en C_1-C_6)alcoxy en C_1-C_6, un phénylalcoxy en C_1-C_6, un nitrophénylalcoxy en C_1-C_6, un alcanoyl(en C_1-C_6)oxy, un benzoyloxy, un fluorènecarbonyloxy, un alcoxy(en C_1-C_6)carbonyloxy, un phénylalcoxy(en C_1-C_6)carbonyloxy, un halophénylalcoxy(en C_1-C_6)carbonyloxy ou un trialkyl(en C_1-C_6)silyloxy, et

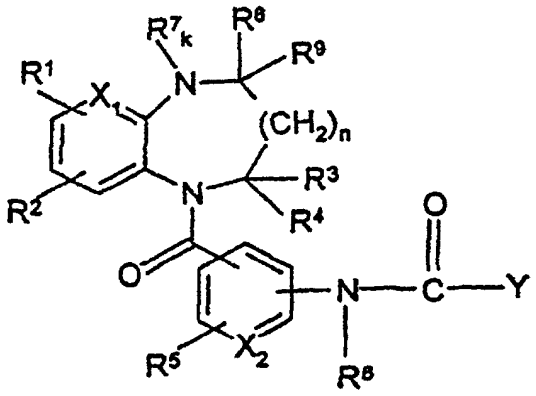
R^7_j est un alkyle en C_1-C_6 substitué avec un hydroxy, ou

p) faire réagir un composé de formule :



(Iu)

ou son sel avec un agent oxydant pour fournir un composé de formule :

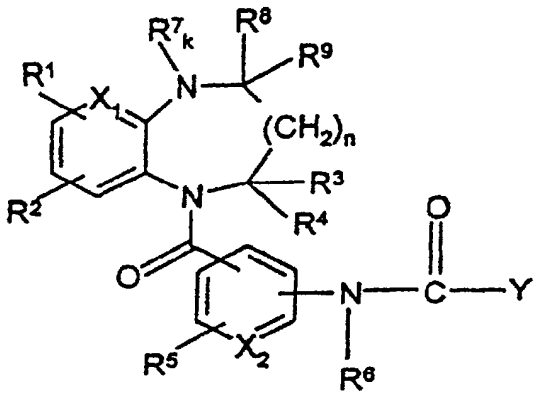


(Ix)

ou son sel,
dans les formules ci-dessus,

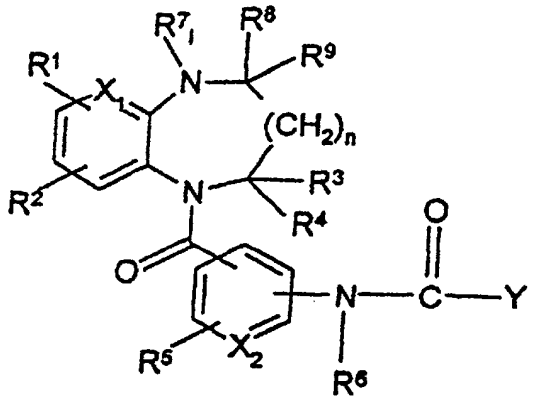
R^1, R^2, R^3, R^4, R^5, R^6, R^7_j, R^8, R^9, X_2, Y et n sont chacun tels que définis ci-dessus, et
R^7_k est un alkyle en C_1-C_6 substitué avec un formyle, ou

q) faire réagir un composé de formule :



(Ix)

ou son sel avec une dialkyl(en C_1-C_6)amine, une pipéridine ou une N-alkyl(en C_1-C_6)pipérazine en présence d'un agent réducteur pour fournir un composé de formule :

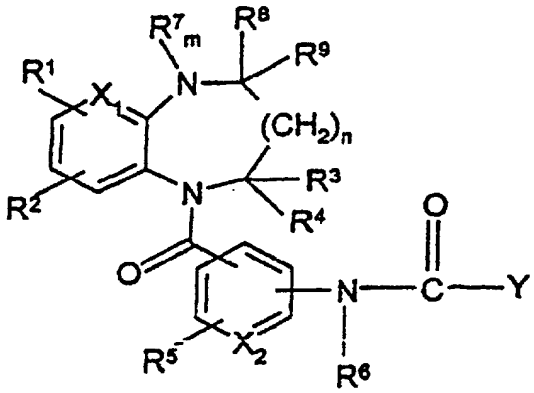


(Iy)

ou son sel,
dans les formules ci-dessus,

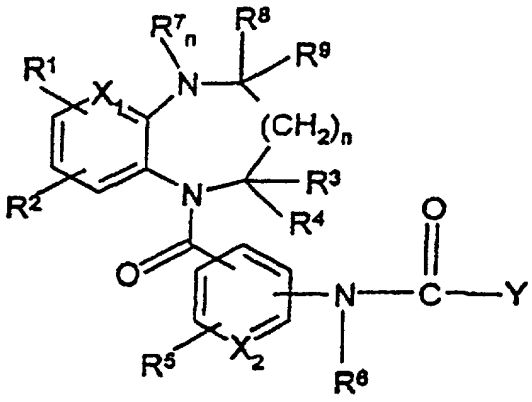
R^1, R^2, R^3, R^4, R^5, R^6, $R^7{}_k$, R^8, R^9, X_1, X_2, Y et n sont chacun tels que définis ci-dessus, et
$R^7{}_l$ est un alkyle en C_1-C_6 substitué avec un dialkyl(en C_1-C_6)amino, un pipéridyle ou un N-alkyl(en C_1-C_6)pipérazinyle, ou

r) soumettre un composé de formule :



(Iz)

ou son sel à une réaction d'acylation pour fournir un composé de formule :

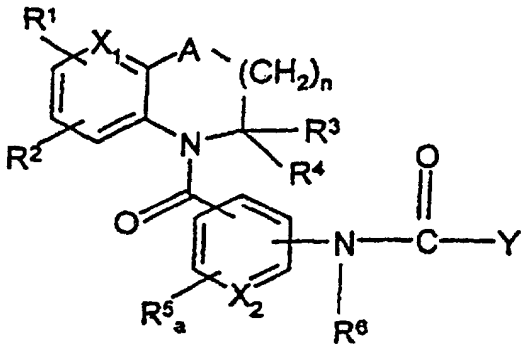


(I-1)

ou son sel,
dans les formules ci-dessus,

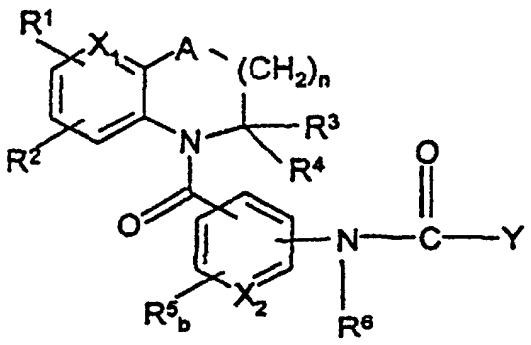
R^1, R^2, R^3, R^4, R^5, R^6, R^8, R^9, X_1, X_2, Y et n	sont chacun tels que définis ci-dessus,
$R^7{}_m$	est un alkyle en C_1-C_6 substitué avec un N-[hydroxyalkyl(en C_1-C_6)]pipérazinylcarbonyle, et
$R^7{}_n$	est un alkyle en C_1-C_6 substitué avec un N- [alcanoyl (en C_1-C_6) oxyalkyl (en C_1-C_6)]pipérazinylcarbonyle, ou

t) faire réagir un composé de formule :



(I-4)

ou son sel avec un halogénure d'alkyle en C_1-C_6 ou son sel, où l'alkyle en C_1-C_6 peut être substitué avec un alkyl(en C_1-C_6)amino, en présence d'une base pour fournir un composé de formule :

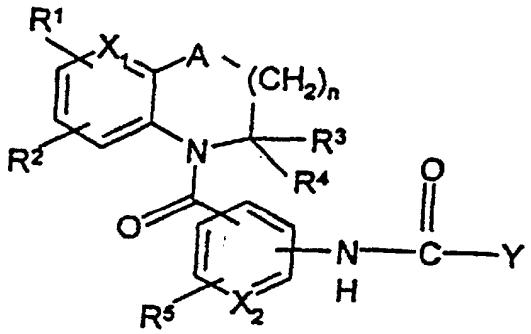


(I-5)

ou son sel,
dans les formules ci-dessus,

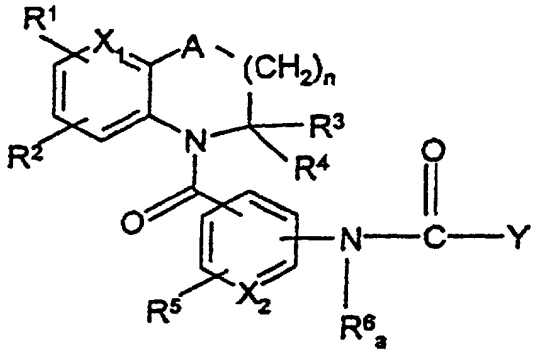
R^1, R^2, R^3, R^4, R^6, A, X_1, X_2, Y et n	sont chacun tels que définis ci-dessus,
$R^5{}_a$	est un hydroxy, et
$R^5{}_b$	est un alcoxy en C_1-C_6 éventuellement substitué avec un alkyl(en C_1-C_6)amino, ou

u) faire réagir un composé de formule :



(Ia)

ou son sel avec un agent alkylant ou acylant pour fournir un composé de formule :

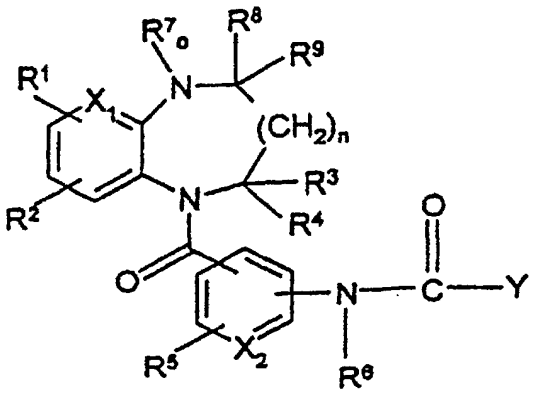


(I-6)

ou son sel,
dans les formules ci-dessus,

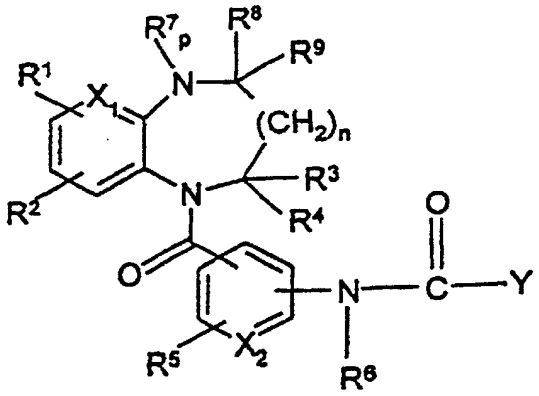
R^1, R^2, R^3, R^4, R^5, A, X_1, X_2, Y et n	sont chacun tels que définis ci-dessus, et
$R^6{}_a$	est un alkyle en C_1-C_6 ou un alcoxy(en C_1-C_6)carbonyle, ou

v) faire réagir un composé de formule :



(I-7)

ou son sel avec un halogénure d'alkyle en C_1-C_6 pour fournir un composé de formule :



(I-8)

ou son sel,
dans les formules ci-dessus,

R^1, R^2, R^3, R^4, R^5, R^6, R^8, R^9, X_1, X_2, Y et n	sont chacun tels que définis ci-dessus,
$R^7{}_o$	est un alkyle en C_1-C_6 substitué avec un N-alkyl(en C_1-C_6)pipérazinylcarbonyle, et
$R^7{}_p$	est un alkyle en C_1-C_6 substitué avec un N,N-dialkyl(en C_1-C_6) pipéraziniocarbonyle.

8. Composition pharmaceutique comprenant un composé de la revendication 1, en tant qu'ingrédient actif, en association avec un support ou un excipient essentiellement non toxique pharmaceutiquement acceptable.

9. Composé de la revendication 1 pour utilisation comme médicament.

10. Composé de la revendication 1 pour utilisation dans le traitement et/ou la prévention d'une hypertension, d'une insuffisance cardiaque, d'une insuffisance rénale, d'un oedème, d'ascites, d'un syndrome de sécrétion inappropriée de vasopressine, d'une cirrhose hépatique, d'une hyponatrémie, d'une hypokalémie, d'un trouble diabétique ou de la circulation.

11. Utilisation d'un composé de la revendication 1, pour la fabrication d'un médicament pour traiter et/ou prévenir une hypertension, une insuffisance cardiaque, une insuffisance rénale, un oedème, des ascites, un syndrome une sécrétion inappropriée de vasopressine, une cirrhose hépatique, une hyponatrémie, une hypokalémie, un trouble diabétique ou de la circulation chez les êtres humains ou les animaux.